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TETANUS IN CHILDHOOD

WITH SPECIAL REFERENCE TO TREATMENT

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When in 1936 one of the physicians on the staff of the Children's Hospital expressed surprise that several consecutive patients with tetanus had recovered during that year, the remark prompted a review of the cases of tetanus observed in that hospital since 1921. The present communication is concerned with those and with subsequent cases. The small number of cases involved cannot be subjected to detailed statistical analysis, and the many uncontrolled variables preclude all but the most general conclusions. In spite of these drawbacks, I feel that certain valid observations have been made and that their implications are of such grave import as to warrant reporting.

REVIEW OF CASES

Although the primary concern of this report is with the treatment of tetanus in children, it is well to become acquainted with the types of cases under discussion. To that end a brief clinical review (largely tabular for the sake of brevity) of the 28 cases under consideration is presented. For the purposes of this study even an abbreviated presentation of individual protocols does not seem necessary. Because the hospital does not maintain an emergency unit for receiving patients injured in accidents, in none of the cases was the disease the result of a mangling street accident. Rather the cases represent a fair cross section of tetanus among children as it is encountered in private practice and in practice in children's hospitals.

Sex.—Twenty-two of the 28 patients were males. This general sex incidence is found in all reported series of cases (except those dealing with newborn children) and is, of course, due to the rough and outdoor play indulged in by boys.

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Age.—The ages of the patients ranged from 2 to 13 years. In over 50 per cent of the cases the tetanus occurred between the ages of 3 and 8 years. It is during these years that children are likely to run about barefooted and are most devoid of discretion while at play.

Source of Infection.—In only 15 cases was the source of infection ascertainable. In 46 per cent of the cases there was no single wound or abrasion on which the infection might be blamed. So trivial are many of the wounds that give rise to tetanus in children that they arouse no concern at the time they are inflicted. In other words, there is no opportunity for prophylaxis, for no exposure is recognized. The types of wound in the 15 cases in which the wounds were evident are shown in table 1.

TABLE 1.—*Sources of Infection in Fifteen Cases of Tetanus*

Source of Infection	Number of Cases
Cut	3
Burn	1
Nail	3
Thorn	1
Splinter	2
Blister	1
Fracture	4

TABLE 2.—*Period of Incubation in Eleven Cases of Tetanus*

Period of incubation, days	7	8	9	10	11	12	13	14	15
Number of cases	2	3	0	2	3	0	0	1	0

Site of Infection.—In almost 50 per cent of the cases in which the site of infection was identified, it was in the foot. The 4 compound fractures were in the forearm. The hand (1 case), the head (1 case) and the buttocks (2 cases) were also shown to be sites of infection.

Period of Incubation.—It has long been recognized that a short period of incubation in tetanus indicates a severe infection and consequently poor prognosis. Contrarily, an extremely prolonged period of incubation is looked on as a good prognostic omen. In 17 of the 28 cases the period of incubation was unknown. The length of time from the infliction of the wound until the appearance of symptoms in the remaining 11 cases is shown in table 2.

Prophylaxis.—In this series of cases the value of orthodox prophylaxis (which is theoretically attractive) was not impressive. Either most of the wounds were of such a minor nature that there was no indication to give antitoxin, or the original injury was entirely overlooked by the child and the mother. In 3 of the 4 cases in which a compound fracture was the site of the infection, the first physician attending the patients administered 1,500 units of tetanus antitoxin.

However, tetanus developed in all 3 children, and 2 of them died. The periods of incubation of their infections were seven, ten and fourteen days. It is therefore apparent that in these 3 cases 1,500 units of antitoxin was woefully inadequate. While it is not a major issue of the present communication, several tentative conclusions in regard to the the prophylaxis of tetanus seem timely:

1. Fifteen hundred units of antitoxin offers insufficient protection to the child with a compound fracture.

2. Fifteen hundred units of tetanus antitoxin apparently protects a child with a minor wound, for in the past eighteen years no child who has received antitoxin for such a wound has been admitted to the hospital with tetanus.

3. Most tetanus, as it is seen in a children's hospital, arises from wounds which are of such a trivial nature that the physician and often

TABLE 3.—*Chief Complaints in Twenty-Eight Cases of Tetanus*

Complaint	Number of Cases
Trismus	18
Convulsions	7
Abdominal pain	7
Stiff neck	5
Stiff gait	5
Backache	8
Local spasm	2
Spasticity	6
Dysphagia	3

the mother are not consulted by the child. The hope of reducing still further the morbidity of tetanus must then lie in the active immunization of large groups of children by means of tetanus toxoid.

Symptoms.—A detailed discussion of the various symptoms appearing during the course of tetanus would contribute little to the value of the present study. Table 3 shows the principal complaints of the patients in the present series. Several facts, I believe, are noteworthy. Every symptom of tetanus is due to either persistent or intermittent muscular spasm. Trismus, the classic symptom of tetanus, was noted in only 67 per cent of the cases up to and including the time of the patients' admisison to the hospital. Abdominal pain and backache each occurred in more than 25 per cent of the cases. Although stiff gait was a prominent symptom in only 5 cases, it was the first and presenting symptom in several of them. Most typically, the muscular spasm involves the masseter muscles, but it may, by affecting principally other groups of muscles, distort the usually clear clinical picture of tetanus.

Examination of the records of the 10 patients who entered the hospital without the history or finding of trismus reveals that the presenting symptoms were readily referable to the same type of muscular spasm

that causes trismus but that the spasm merely involved other groups of muscles. The chief complaints of these 10 patients are shown in table 4. The 3 patients with severe periodic spasms of abdominal pain and the 2 patients with excruciating backache presented harassing diagnostic problems until a suspicion of tetanus magnified some other symptom that previously had been overlooked.

Physical Findings.—The physical findings in cases of tetanus have been described many times. The disease is characterized by intermittent or persistent spasm of various groups of muscles. This spasm may vary from slight rigidity of small groups of muscles to horribly painful and exhausting convulsive contractures of practically all of the

TABLE 4.—*Presenting Symptoms in Ten Cases in Which Trismus Was Not Present*

Symptoms	Number of Cases
Dysphagia	1
Backache	2
Stiff gait	2
Spasticity	2
Abdominal pain	3

TABLE 5.—*Complications in Twenty-Eight Cases of Tetanus*

Complication	Number of Cases
Pneumonia	2
Bronchitis	1
Stomatitis	1
Contracture	1
Purpura	1
Otitis media	1
Acute pyuria	2
Barbitalism	1
Vertebral compression	9

voluntary muscles of the body. Although one usually thinks of the "locked jaw," risus sardonicus and boardlike abdomen as characteristic findings in tetanus, some or all of these particular muscular spasms may be absent. Throughout the course of the disease the sensorium remains brutally clear.

Laboratory Findings.—Except in those instances in which smears or cultures of the wound may prove the diagnosis by revealing the presence of Clostridium tetani, laboratory studies are of little value. The leukocyte and differential counts vary according to the nature of the primary wound and the amount of secondary infection present in it. The cerebrospinal fluid is normal, except that the pressure may be increased if the patient is having spasms.

Complications.—With one notable exception, the complications in this series of cases were largely pyogenic (table 5). Nine of the 13 patients

who recovered had compression deformities of one or several dorsal vertebrae.[1] This striking complication of tetanus was first described and studied in Germany and was then reviewed in the American literature by Roberg.[2] Drs. Stewart and Karshner and I have reported these 9 cases in some detail.[3] Figure 1 is a roentgenogram of the patient in 1 of these cases. In a high percentage of cases of tetanus among children, definite compression deformities of dorsal vertebrae develop. Usually the abnormality is manifested early by pain or tenderness over

Fig. 1.—Roentgenogram of lateral thoracic portion of the spine, showing definite deformities of compression of the fifth, sixth, seventh and eighth vertebrae.

the affected region. In many cases of this series, however, no symptoms occurred, and the complication was discovered only because it had

1. An additional patient who recovered, seen after this series was studied, also had vertebral deformities. At present, then, 10 of 14 patients (over 70 per cent) suffered from this complication.

2. Roberg, O. T., Jr.: Spinal Deformity Following Tetanus and Its Relation to Juvenile Kyphosis, J. Bone & Joint Surg. **19**:603 (July) 1937.

3. Dietrich, H. F.; Karshner, R. G., and Stewart, S.: Tetanus and Lesions of the Spine in Childhood, J. Bone & Joint Surg. **22**:43 (Jan.) 1940.

become a routine practice to take roentgenograms of the dorsal vertebrae in all cases of tetanus. According to the earlier writers, in those cases in which the complication is not discovered during the course of the disease or during the convalescence, pain or kyphosis may appear months or even years later. The treatment is orthopedic, and by the use of hyperextension and jackets during the patient's convalescence from the tetanus, any serious permanent deformity has apparently been prevented in this series. However, the results will need to be checked in at least five years before definite claims can be made. Because the lesion is due to the severe tonic muscular contractions, it is possible that a more uniform and a smoother sedation may prevent the complication in a high percentage of cases. It is of interest that similar lesions have recently been reported following even single convulsions induced with metrazol.[4]

Admitting Diagnoses.—From a study of the chief complaints of these patients it is evident that the admitting diagnosis would sometimes be doubtful. Actually the diagnosis of tetanus was made in only 17 of the 28 cases at the time of the first examination. However, the initial diagnostic errors were soon rectified, and there is, I believe, no reason for being ashamed of the series from the standpoint of diagnosis.

TREATMENT

I cannot say the same for the record of the treatment in these cases. But first, a few words of introduction. Until the advent of antitoxin, the treatment of tetanus was largely symptomatic. When tetanus antitoxin was first described an optimistic hope that the problem of the therapy of tetanus was solved swept through the medical world. It was not long, however, before it became apparent that because the toxin-nerve cell union was not disrupted by antitoxin,[5] serum therapy was disappointing. In this connection it is of interest that during the nineteenth century, particularly in France, tetanus was treated with subcutaneous injections of bovine brain in an attempt to bind circulating toxin. Then a wave of "serum nihilism" swept through the literature, and attention was again directed at the symptomatic relief of the convulsive spasms. Scores of sedatives received intense study and had great popularity. Fairly recently, with the publication of several large series of cases with low rates of mortality,[6] in which extremely large

4. Polatin, P.; Friedman, M. M.; Harris, M. M., and Horwitz, W. A.: Vertebral Fractures Produced by Metrazol-Induced Convulsions in Treatment of Psychiatric Disorders, J. A. M. A. **112**:1684 (April 29) 1939.

5. Ransom, F.: A Modern View of Tetanus, Lancet **2**:928 (Dec. 22) 1917.

6. (*a*) Bower, A. G.; Best, E. J., and Vener, H. I.: Tetanus, California & West. Med. **48**:191 (March) 1938. (*b*) Yodh, B. B.: Further Observations on the Treatment of Tetanus, Brit. M. J. **1**:855 (April 24) 1937.

doses of antitoxin had been given, dependence on serum revived. Most of these reports are of series of cases in which the patients include both adults and children. However, Patterson [7] reported a group of 26 cases of tetanus in children in which he gave 100,000 to 2,000,000 units of antitoxin intravenously and intramuscularly. His gross mortality rate was 26.9 per cent. If one can accept the work of Cole and Spooner and of Abel (to be discussed subsequently), there is certainly no justification for such heroic extravagance. It becomes evident that a complete résumé of the literature on the treatment of tetanus would be monumental, confusing, definitely contradictory and of little aid to the physician attempting to treat a single child with tetanus. I shall not attempt it.

TABLE 6.—*Mortality in Cases of Tetanus Before and After 1933*

Year of Occurrence of Tetanus	Number of Patients Who		Year of Occurrence of Tetanus	Number of Patients Who	
	Recovered	Died		Recovered	Died
1921	0	1	1933	2	1
1922	0	1	1934	1	0
1923	0	0	1935	1	0
1924	0	0	1936	1	0
1925	1	0	1937	3	0
1926	0	1	1938	4	0
1927	1	1			
1928	1	3			
1929	0	2			
1930	0	1			
1931	0	0			
1932	0	2			
Total	3	12	Total	12	1
	Mortality, 80%			Mortality, 8%	

The present series of cases is too small and the number of uncontrolled variables is too large to permit a statistical evaluation of the results of treatment. This need not rob the experience of its practical value. The most casual glance at table 6 must convince one that the mortality rates in the groups of cases are significantly different. In such a small series of cases it is perhaps more fruitful to examine the deaths than the recoveries. While I cannot directly and positively account for the excellent recovery rate in the years 1933 to 1938, I can, I believe, show that the appalling mortality rate from 1921 through 1932 was the direct result of orthodox treatment. The inference is obvious. The improved rate of mortality in recent years must be due in part to the fact that the treatment in the second group of cases has not proved fatal to as many patients.

7. Patterson, A. E.: Tetanus: Its Diagnosis and Treatment, M. J. Australia 1:832 (June 28) 1930.

CASES IN WHICH DEATH OCCURRED

There are a number of factors that are worth investigating in those cases in which the patient died.

Time of Death.—In the usual analysis of cases it is customary to consider the duration of the disease from the onset of symptoms up to the time of death. Such a study in this series would be relatively sterile, for there is a much more important relationship. Figure 2 shows the number of hours that the patients lived after receiving their first dose of serum, either intrathecally or intravenously (or both). Most of these patients walked into the clinic with moderately severe or with mild tetanus. It made no difference whether they had been sick one day or ten days, whether the period of incubation had been seven days or fourteen or whether the initial wound was caused by a nail or a blister, they all died within thirty-six hours of their first treatment. Eleven of the 13 died within three to fourteen hours of the time they first received serum. Every patient had been tested for cutaneous sensitivity to horse serum.

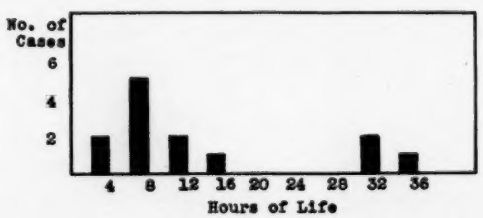

Fig. 2.—Hours of life after first treatment in 13 cases of tetanus in which death occurred.

The records of the temperature and pulse in 4 exemplary cases are shown in figure 3. The first 3 records show a dramatic and fatal reaction immediately after treatment. In the first and third cases serum was given intravenously and intrathecally; in the third case a single intravenous injection of 10,000 units of antitoxin was administered. The patient in the fourth case survived treatment the longest. He suffered an extremely severe reaction after his first treatment but managed somehow to live through the night. A second intravenous and intrathecal injection on the following morning resulted in another reaction, which proved fatal. Every child who died showed a reaction similar to those illustrated; in the second and the fourth case (fig. 3), respectively, the reactions were the least rapidly fatal.

Character of the Reaction.—From a clinical standpoint the reactions are striking. The picture of tetanus, with clear mentality, frequent tonic spasms, normal or slightly elevated temperature and moderately elevated pulse rate, is suddenly changed to resemble certain phases of bulbar

poliomyelitis or some other disease with medullary pressure or edema. Coma, startling hyperpyrexia, extreme tachycardia, stertorous and irregular respiration and a cessation of the tonic convulsions compose the new clinical picture. The face becomes ashen, and perspiration is frequently profuse. The extremities are often cold and mottled. Unswallowed secretions lend a gurgling quality to the nearly terminal breathing. Then death comes, but obviously not from tetanus.

Cause of Death.—The underlying causes of death are probably several; the immediate lethal factor appears to be medullary (and cerebral) edema. In 6 cases in which autopsies were done this edema was readily demonstrable. Because of the rapidity with which the clinical reaction

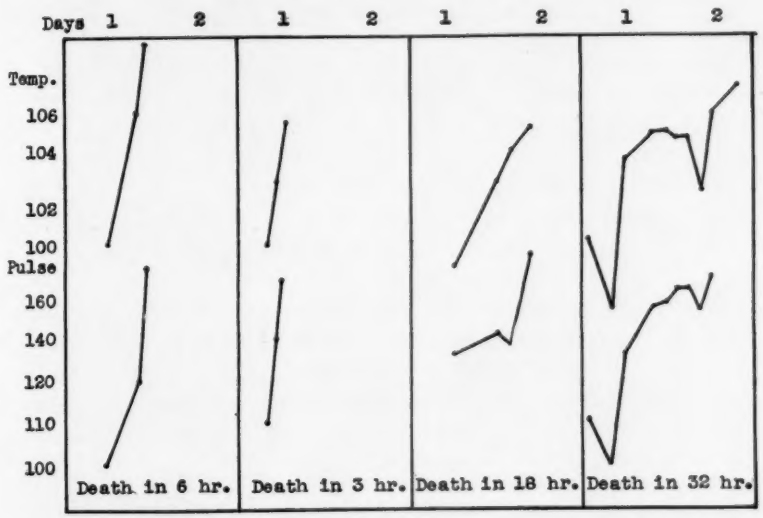

Fig. 3.—Untoward reactions to therapy in 4 cases of tetanus in which death occurred.

followed the intravenous or intrathecal administration of serum, it seems reasonable to assume that the edema was the result of some reaction to the serum. If some of these reactions are allergic, then epinephrine should prevent them; in the few cases in which it was tried the drug did not appear to be of great value. Only further observation will clarify this point.

In addition to this possible danger, the intrathecal administration of serum offers another hazard. Any horse serum administered into the subarachnoid space incites a sterile meningitis; the latter may well account for the medullary edema when serum is given by either the lumbar or the cisternal route. Table 7 shows the cell count in 4 cases in which lumbar punctures were done before and eight to twenty

hours after the introduction of tetanus antitoxin into the subarachnoid space. In each instance an acute inflammatory process was induced by the serum.

CASES IN WHICH RECOVERY OCCURRED

Brief consideration of the treatment with serum and the reactions observed in the last 13 cases (table 8) will help to emphasize the relation between the route by which the serum is administered and the prob-

TABLE 7.—*Cell Count of Cerebrospinal Fluid, Showing Inflammatory Reaction Incited by the Intrathecal Administration of Antitoxin in Four Cases of Tetanus*

Case		Before Administration of Serum	After Administration of Serum
1	Cells	1	1,000
	Polymorphonuclears	0	98%
2	Cells	2	4,190
	Polymorphonuclears	0	89%
3	Cells	1	800
	Polymorphonuclears	0	90%
4	Cells	1	1,208
	Polymorphonuclears	0	97%

TABLE 8.—*Results of Serum Therapy in Thirteen Cases of Tetanus, 1933-1938*

Case	Method of Administration of Serum			Reaction	Result
	Intrathecally	Intravenously	Intramuscularly		
1	..	+	..	Fatal	Death in 3 hr.
2	+	+	+	Severe	Recovery
3	+	+	+	Severe	Recovery
4	+	+	+	Severe	Recovery
5	+	+	+	Severe	Recovery
6	..	+	+	Severe	Recovery
7	..	+	+	Severe	Recovery
8	..	+	+	Moderate	Recovery
9	..	+	+	Moderate	Recovery
10	..	..	+	None	Recovery
11	..	..	+	None	Recovery
12	..	..	+	None	Recovery
13	..	..	+	None	Recovery

ability of severe reaction. It will be noted that all 4 patients receiving serum both intrathecally and intravenously had severe reactions. These reactions differed from the fatal ones in only a minor quantitative degree, and the patients managed to survive. Figure 4 shows the records of patients in 2 such cases. The record in figure 4 *A* is that of a patient who suffered a severe reaction after intrathecal and intravenous administration of serum. On the day after the first treatment 7 minims (0.431 cc.) of epinephrine was given intravenously at the same time as the serum. The reaction was more severe than that after the first treat-

ment, and the patient nearly died. However, as in all the cases in which the patient recovered, after a few critical hours the reaction subsided and the clinical picture reverted to one of tetanus. Figure 4 *B* shows the changes in temperature and pulse in one of the most interesting and satisfying cases in the series. When the patient displayed a frightening and nearly fatal reaction a few hours after the intravenous administration of serum, it was felt, on the basis of previous observations, that he probably had cerebral edema. The use of sedatives was stopped, and a 30 per cent solution of sucrose was given intravenously. There was immediate improvement in the patient's appearance, but his condition remained grave. After the repeated administration of hypertonic sucrose solution the temperature and pulse suddenly dropped, and the patient again showed the clinical signs of tetanus.

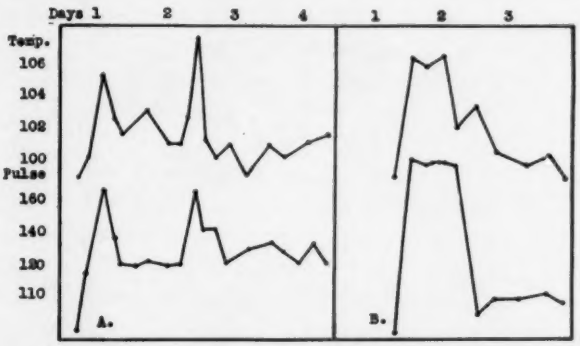

Fig. 4.—Untoward reactions to therapy in 2 cases of tetanus in which recovery occurred.

It will be noted that the patients in cases 10 to 13 inclusive (table 8) received no intrathecal or intravenous injections of serum and were the only patients in the entire series who did not show some untoward reaction following serum therapy.

Sedation.—No attempt will be made to undertake a comprehensive discussion or an actual analysis of the role of sedatives in the results in these two groups of cases. It is my personal opinion that serum and sedatives are each complementary but are not self-sufficient units in the therapeutic armamentarium. Serum should be used to prevent further toxin fixation; sedatives alone can combat the effects of toxin already bound in the central nervous system. All theoretic considerations to one side, it is inconceivable to me that any clinician can see a child in the torture of a tetanic spasm and blithely say, "Never mind the sedative; just get in another 100,000 units of antitoxin." I once asked a youngster who had just recovered from tetanus what it felt like to have the disease. His answer left little doubt as to the agonies suffered

by these patients. He said, "Have you ever had a bad cramp in your leg? Well that's the way it feels all over!" In addition to any humane virtues, sedatives have the power to spare the patient the exhaustion that may be the deciding factor in the outcome of the disease.

Table 9 suggests the major differences in sedation used in the two groups of cases that I have been discussing. A voluminous literature attests the virtues of magnesium sulfate, paraldehyde, chloroform, amytal and avertin with amylene hydrate, and no critical evaluation of their merits will be attempted. The ideal sedative in cases of tetanus should provide rapid and deep sedation without loss of cough and pharyngeal reflexes and with minimal depression of respiration. Further, the drug should be rapidly excreted and of sufficiently low toxicity to permit its continued use in large doses for considerable periods. Its administration should be possible by other routes than the oral. Actually, in cases of severe tetanus it is often impossible to maintain safely the desired effect

TABLE 9.—*Sedatives Used in Treatment of Tetanus*

1921-1932	1933-1938
Drug	Drug
Morphine sulfate	Paraldehyde
Chloral hydrate	Amytal
Magnesium sulfate	Avertin with amylene hydrate
Paraldehyde	Seconal
Dose: small	Dose: very liberal

with a single drug and several must be used in rotation. My most recent experience has been with seconal (sodiumpropylmethylcarbinylallylbarbiturate). During the course of a clinical appraisal of this sedative [8] in which over 3,500 doses were administered, I decided to try it in the treatment of tetanus. Doubts were entertained of its possible value in the latter disease because of the short duration of its action and the extreme rapidity of its destruction. Paradoxically, the drug has proved almost ideal in the 3 cases in which it has been used, and the rapidity of its destruction appears to be a definite virtue. In 2 of these 3 cases it was the only sedative used. In the third case other sedatives were employed, but seconal proved at least as effective as any. Convulsions have been controlled rapidly and well, and yet the preservation of pharyngeal and cough reflexes has eliminated the fear of aspiration pneumonia. Even one or two hours after the administration of "knock-out doses" (i. e., 3 to 4 grains every three or four hours to a 5 year old child) it has been possible to arouse the patient to take fluids by mouth. The

8. Dietrich, H. F.: Seconal as a Sedative in Infancy and Childhood, to be published.

extreme rapidity of its action, even when given by rectum, has made the drug extremely valuable. I am certain that tetanus cannot be controlled in all cases by seconal alone, but in the light of my abbreviated experience with it in cases of tetanus, I feel that the drug will prove to be at least one of the most valuable sedatives.

COMMENT

In reviewing the records of these 28 cases of tetanus I did not start out with the intention of proving anything. Certain glaring facts revealed in that review, however, so impressed me that I felt compelled to record them. A high percentage of children who received serum intrathecally or intravenously had severe reactions in which the picture of tetanus was eclipsed by one of some bulbar disease. Death followed in a few hours and was apparently due to medullary and cerebral edema. From this series of cases it must be concluded that such fatal reactions occur more frequently in children than they have been reported to occur in adults. Why? The reason is not known. Perhaps the immature central nervous system is more liable to and sensitive to pressure than the adult one, or there is physically less room for medullary swelling in the juvenile than in the adult subarachnoid space. It is known that with certain streptococcic infections [9] the accompanying cerebral edema is both more prominent and much more frequently fatal in infants and children than it is in adults. To return to the problem of tetanus, reactions practically never occur after intramuscular injections of serum.

There are, then, in dealing with children one safe route and two dangerous ones for the administration of tetanus antitoxin. What of their relative efficacies? In the past Abel has repeatedly demonstrated that tetanus toxin, once bound in the central nervous system, is not affected by antitoxin. Although one of the last papers by Abel and his co-workers [10] presented some evidence to the contrary, this evidence is not yet, and probably never will be, applicable to clinical tetanus. Actually serum is given only to neutralize circulating toxin and toxin which may be liberated in the future. The subarachnoid route is an extremely indirect one by which to introduce tetanus antitoxin into the blood and interstitial fluids. Because time is an important factor,[11] the

9. (*a*) Farber, S.: Fulminating Streptococcus Infections in Infancy as a Cause of Sudden Death, New England J. Med. **211**:154 (July 26) 1934. (*b*) Rector, J. M.: Fulminant Streptococcus Sepsis in Infancy, J. Pediat. **10**:592 (May) 1937.

10. Abel, J. J.; Hampil, B.; Jonas, A. F., Jr., and Chalian, W.: Researches on Tetanus: The Time Required for the Fixation of a Fatal Quantity of Tetanus Toxin, Bull. Johns Hopkins Hosp. **62**:522 (May) 1938.

11. Abel, J. J., and Chalian, W.: At What Point in the Course of Tetanus Does Anti-Tetanic Serum Fail to Save Life? Bull. Johns Hopkins Hosp. **62**: 610 (June) 1938. Abel, Hampil, Jonas and Chalian.[10]

intravenous route is theoretically the ideal one for the administration of at least the first dose of serum. It has been shown in studies on the absorption of pneumococcus and other serums that there is a lag of from twelve to twenty-four hours in the concentration of antibodies in the blood when the serum is given by the intramuscular rather than the intravenous route. However, I have observed cases in which death occurred from a single dose of serum administered intravenously, and so one need not feel too anxious to base therapy on theoretic advantages alone. Three courses present themselves. The first course, which was followed in the last 4 cases of the present series (and in a subsequent case in which recovery occurred, which is not included in this series), is to assume the risk of slow effect rather than the danger of intravenous injection of serum and to give antitoxin only intramuscularly. This method is not theoretically ideal and might permit a fatal spread of toxin in a case in which the condition was critical before the concentration of antitoxin in the blood reached an adequate titer. The second possibility is to give one dose of antitoxin and epinephrine intravenously and then follow it by the intramuscular administration of serum to maintain the concentration of antitoxin in the blood. This practice should provide maximal effectiveness but is not free from danger. There is certainly no theoretic or practical reason for repeating the single dose intravenously if repeated doses of serum are given intramuscularly to maintain the titer of the antitoxin. Cole and Spooner [12] have shown that 25 per cent of a single large dose of antitoxin given intravenously is still demonstrable in the blood seven days after injection. The third possible plan of treatment, I believe, will prove to be the ideal one. It is as yet untried. Dr. Clarence Hyland, of the Serum Center of the Children's Hospital, has suggested making human tetanus antitoxin by immunizing donors with tetanus toxoid, and preparations are being made to do so. With such a serum available, it would be possible to give first a single dose of human serum intravenously without fear of an untoward reaction. The concentration of tetanus antitoxin in the blood could then be maintained safely by daily doses of orthodox tetanus antitoxin intramuscularly. The requisites of ideal serum therapy would thus be satisfied. An adequate concentration of antitoxin could be rapidly and safely induced and subsequently maintained without danger to the patient.

When one reads the literature on tetanus it immediately becomes apparent that there are widely divergent opinions on the question of the value of sedatives. More pertinent, it is also obvious that those writers who warn against the use of large doses of sedatives are the

12. Cole, L., and Spooner, E. T. C.: The Treatment of Tetanus, with Observations on the Fate of Injected Antitoxin, Quart. J. Med. **4**:295 (July) 1935.

same who employ maximal doses of antitoxin by the intrathecal and intravenous routes. From my observations one inference is unavoidable. During a severe reaction to antitoxin, sedatives are not symptomatically indicated and may actually cause death by aggravating existing symptoms. However, if serum is given only by routes which do not excite "bulbar reactions," sedatives are of great value in tetanus. In other words, as long as one does not alter the picture from one of tetanus to one of "bulbar disease," sedatives are indicated and safe. The patient is spared the pain and exhaustion of repeated, severe spasms, and death from prolonged spasm of respiratory and other vital muscles is precluded.

Sedation is clearly indicated before any other therapeutic or diagnostic procedures are undertaken. Antitoxin should then (in severe cases) be given intravenously to neutralize rapidly preformed toxin and intramuscularly to provide a slower but more continuous source of antitoxin. The focus of infection should next be surrounded with antitoxin and then widely opened and thoroughly cleaned or debrided and left open. Thereafter there are three important phases to the treatment of tetanus. The first is to spare the patient with adequate sedation and quiet surroundings. The second is to provide a continuous but moderate supply of antitoxin to neutralize any new toxin liberated. This is most safely done entirely with serum administered intramuscularly, and probably 10,000 to 20,000 units a day for two to four days is adequate.

I have not discussed the question of the total dosage of antitoxin that is required, for there is little concrete evidence on which to base such a discussion. If it is conceded that antitoxin can only neutralize circulating toxin, then the large doses that have sometimes been recommended seem superfluous. Certainly many patients with severe tetanus have recovered with a total of 40,000 to 60,000 units of antitoxin. Finally, during the critical first three to seven days reasonable amounts of fluid and nourishment must be administered. If the patient can take them, frequent, relatively small, concentrated, liquid feedings should be given by mouth. After seeing 2 children with tetanus (at the Boston Children's Hospital) in whom unilateral atelectasis developed from the aspiration of large milk curds which had been vomited, I have preferred to give evaporated milk or other milk with soft (small) curds. This, supplemented with sugar and perhaps egg, provides a sustaining diet. So far as I have been able to ascertain, no child with tetanus has ever died of starvation. The important factor about feeding, then, is to make it safe. If food by mouth cannot be given without choking and gagging, one must resort to feeding by tube or to fluids given parenterally. Dextrose administered intravenously

and saline solutions given subcutaneously will readily sustain the patient with tetanus through the few really critical days.

Ever since the foregoing ideas on the treatment of tetanus began to take shape, one question has perplexed me. How can this rather nihilistic attitude toward serum be reconciled with the fact that several series of cases have been reported showing a decrease in mortality with the use of increasingly large doses of antitoxin intrathecally and intravenously? It cannot be entirely reconciled. Several explanations have suggested themselves, however. The first, and perhaps the least tangible, is that childlren react differently to serum (and sudden cerebral edema) than do adults. Most of the reported series of cases in which large doses of serum have been used have come from general hospitals and have included adults as well as children. The second possible answer concerns a previously overlooked statistical fallacy. Many years ago some zealous physician decided that deaths which occurred within twenty-four hours after he had first seen the patient should not

TABLE 10.—*Two Ways of Reporting Mortality Rates*

	Cases	Deaths	Mortality	24 Hour Deaths	Net Deaths	Net Mortality
Total	28	13	46.4%	10	3	16.6%
Group 1	15	12	80.0%	9	3	50.0%
Group 2	13	1	7.6%	1	0	0.0%

be considered in his mortality figures, for he had not had time to give sufficient treatment. So there was evolved "net mortality"; i. e., the percentage of patients who died, but who lived more than twenty-four hours. The "twenty-four hour deaths" were not included in tabulating statistics. By this method of computation the net mortality rate before an efficient firing squad should be 0 per cent. Table 10 shows how the application of this principle would affect mortality figures. The net mortality rate for the entire series (16.6 per cent) compares with the best figures published, and yet my previous review shows that the treatments actually killed 11 or 12 of the 13 patients who died. When one studies published reports with this idea in mind an interesting and rather tragic observation comes to light. In his first report Yodh [13] recorded the results in a large series of cases. The latter are divided into three groups. Group A embraces the cases seen in his clinic prior to the time when he directed the care. Group B includes 102 cases in which large doses of serum were given intravenously. Because the gross mortality was 63 per cent (65 deaths), he decided to give additional

13. Yodh, B. B.: Observations on the Treatment of Tetanus, Brit. M. J. **2**:589 (Sept. 24) 1932.

serum by the cisternal and lumbar routes. Group C comprises 112 cases in which serum was given by those routes, and in which the gross mortality was 47 per cent (53 deaths). No one can deny some improvement in gross mortality; however, stress is laid on net mortality (40 per cent and 23 per cent, respectively, in groups B and C), as indicating the true improvement in therapy. It is at this point that I would take exception with the author's implications. With the addition of the intrathecal administration of serum to the therapeutic routine, the percentage of patients (among those dying) who died within twenty-four hours rose from 46 to 66 per cent. In other words, with the addition of a dangerous therapeutic procedure, more patients died soon after receiving treatment. I have not singled out this one report because I felt the author was attempting to mislead his readers, but simply because I wanted to stress the skepticism with which figures representing net mortality must be viewed. Discard these so-called twenty-four hour deaths entirely, and an advance in therapy must be assumed. But can one ignore them? I cannot answer for other reports. In my series of cases these deaths were too obviously the direct result of therapy to permit me to say casually, "The patients were too far gone before they came to the hospital." Most of the deaths in this series occurred much sooner than they possibly could have in untreated tetanus. Therefore, it would seem unreasonable to ascribe too much importance to "net mortality" in any condition in which the initial treatment itself has lethal potentialities.

SUMMARY

A series of 28 cases of tetanus in children is reviewed. The initial administration of tetanus antitoxin by vein or into the subarachnoid space was always followed by a severe, and many times by a fatal, reaction. The reaction was characterized clinically by extreme hyperthermia, marked tachycardia, coma, irregular respiration and sudden death. In every instance death occurred within thirty-six hours, and in most cases (84 per cent) within three to fourteen hours, of the first treatment. Pathologically, medullary and general cerebral edema were found. The only 4 patients in the entire series who did not show untoward reactions to serum therapy received serum only intramuscularly; these patients enjoyed uneventful recovery. During the years 1921 to 1932, 12 of 15 children with tetanus died (80 per cent). From 1932 to 1939 there was 1 death in 13 cases (8 per cent). From a review of the records of the cases it is clear that most if not all of the deaths in the first group of cases and the only death in the second group occurred as a direct result of treatment. It would appear that the improved rate of mortality in the second group was due to the more judicious and less enthusiastic use of serum and to the increasing

dependence on sedatives. Refinement of serums in the last few years probably aided in reducing the number of severe reactions. Good fortune played a major role, too, for a number of the children who recovered had severe reactions to serum but managed to survive.

CONCLUSIONS

1. Fifteen hundred units of tetanus antitoxin does not afford adequate prophylaxis in cases with compound fractures.

2. Compression deformities of dorsal vertebrae constitute a common complication (over 60 per cent of the cases) in tetanus.

3. Moderate doses of serum are theoretically adequate in the treatment of tetanus.

4. Intrathecal administration of serum is theoretically unsound and practically dangerous in treating tetanus in children.

5. Intravenous administration of serum may cause fatal reactions, but a single dose is theoretically advantageous.

6. Intramuscular administration of antitoxin is completely safe, and by itself is adequate, except possibly when the tetanus is most severe.

7. Except during the course of reactions to serum administered intravenously and intrathecally, sedatives are safe, highly desirable in large doses, and frequently life-saving in the treatment of tetanus in children.

8. The use of "net mortality" in reporting series of cases of tetanus may obscure the dangers of therapy.

SULFAPYRIDINE IN THE TREATMENT OF PNEUMONIA IN INFANTS AND IN CHILDREN

REPORT ON FIFTY-EIGHT TREATED PATIENTS AND FIFTY-SIX CONTROLS

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PLAN OF STUDY

Selection of Patients.—The 119 patients with pneumonia included in this study were admitted to the Children's Hospital of Philadelphia between Oct. 1, 1938 and May 1, 1939. In each case the diagnosis was made by the admitting officer and the patient assigned to either the control group or the group to be treated with sulfapyridine. Five infants considered moribund at the time of admission were placed in a separate group and treated with sulfapyridine. Of the remaining 114 patients, 58 were assigned to the group to receive treatment and 56 to the control group.

Diagnosis.—The diagnosis was made in each instance by clinical examination. In 5 of the 114 cases in the compared series no roentgenograms were made, but the clinical observations were definite in each instance. No attempt has been made to separate lobar and bronchopneumonia, as in many cases a clinical diagnosis of one was made and the other was reported in the films. A blood culture was made in each case; all the cultures were negative. Sputum was collected in each case. In many sputums pneumococci were found, some of which were typed from blood agar plates with specific serums, but others of which failed to type. Many of the cases in which culture did not yield pneumococci were similar in course and finding to those in which culture yielded definite types. No attempt has been made to correlate types with clinical results because of the small number of cases.

Blood Counts and Urinalyses.—Blood counts were made for all patients at the time of admission to the hospital. For the treated group, counts were repeated at forty-eight hour or shorter intervals during

The sulfapyridine used in this study was furnished by Merck & Co., Inc., Rahway, N. J., and Dr. Harrison F. Flippin, Philadelphia.

From the Department of Pediatrics, School of Medicine, University of Pennsylvania, and the Medical Services of the Children's Hospital.

treatment in order to detect any serious effects on blood formation. For the control group many additional counts were made.

Urinalyses were made for all patients of both groups, and for many of the treated group repeated urinalyses were made.

With the exception of the drug, no difference was made in the treatment of the controls and the treated patients. When oxygen was necessary it was used in either group. Transfusion was used liberally in both groups. No serum was used in any of the cases.

Method of Administration.—Sulfapyridine was administered to the treated group in the following manner: A daily dose of 1.5 grains (0.09 Gm.) per pound of body weight was calculated. This was divided into six or eight daily doses. Treatment was continued for ninety-six hours regardless of temperature. It was stopped only because of severe gastrointestinal irritation or because of a toxic effect on hemoglobin, red cell or white cell formation.

The sulfapyridine was measured and powdered. It was usually given in a small amount (½ ounce [15 cc.] or less) of fruit juice a short while before a meal or feeding. In some instances it was given in milk, cereal, apple sauce or jelly, but it was generally thought that the fruit juice was the best vehicle.

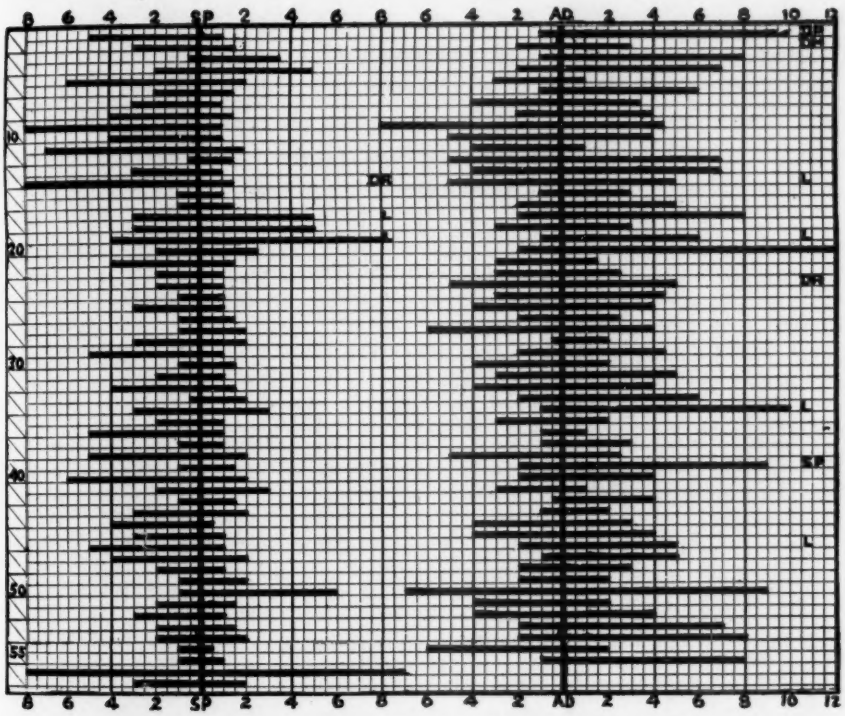
RESULTS

In most instances the drug appeared to have a serum-like effect, precipitating a crisis in twelve to twenty-four hours. The fall in temperature was usually accompanied by lowering of the respiratory rate and loss of the dyspnea. In a few cases, however, in spite of a normal temperature respiratory symptoms persisted, even to the extent of requiring the use of an oxygen tent. In some patients the relief of fever and dyspnea was not accompanied by a feeling of well-being and resumption of activity until the drug was discontinued.

The chart gives a graphic comparison of the treated and the control group of patients. On the left side of the chart the vertical line *SP-SP* indicates the beginning of the administration of sulfapyridine. On the right side the vertical line *AD-AD* indicates the time of the patient's admission to the hospital. Each patient is represented by a horizontal line; the length of this line to the left of the vertical line represents the number of days between onset and treatment in the first group and between onset and admission to the hospital in the control group. The criteria for the determination of the onset were the same with each group. The length of the lines to the right indicates the time in days from the beginning of treatment or from admission to the first normal temperature that remained permanent. It will be seen that this

does not designate the first significant fall in temperature but rather the earliest time of the permanent disappearance of fever. It therefore includes all febrile complications, of which otitis media was, as could be expected, the most frequent.

The course prior to treatment or prior to admission, as the chart shows, was of approximately equal length for the two groups, averaging somewhat less than three days (two and ninety-four hundredths days



The length of the lines to the left of line *SP-SP* indicates the number of days between the onset of the pneumonia as determined by the history and the beginning of treatment with sulfapyridine. Lines to the right of *SP-SP* indicate the number of days between the first dose of the drug and the beginning of a permanent normal temperature. Lines to the left of the line *AD-AD* indicate for the control group, in a similar manner, the number of days between onset and admission to hospital. Lines to the right of this line indicate the days elapsing between admission and the first day of a permanent normal temperature. This method of representation includes all febrile complications during the twelve days after admission. In several instances otitis media occurred at a later date but could not justifiably be considered a complication of the pneumonia. *DR* = delay of resolution; *L* = decline by lysis without complications *DP* = a patient who died of postpertussis pneumonia; *DM* = a patient who died of pneumococcic (type *XIV*) meningitis; *SP* = a patient treated as a control for nine days, then given sulfapyridine, with a permanent fall of temperature in twenty-four hours.

for the 58 treated patients, two and eighty-four hundredths days for the 56 controls). The course following institution of treatment or following admission was materially shortened in the treated group, averaging two days as compared with an average of four and fifty-five hundredths days in the control group.

The total febrile course averaged four and ninety-four hundredths days in the treated group as compared with seven and thirty-nine hundredths days in the control group. In 4 patients of the control group and in 2 patients of the treated group the disease declined by lysis. There was clinical delay of resolution in 1 patient in each group, but in neither of these was the febrile course prolonged.

There were no patients in either group in whom empyema developed. In the control group 2 patients died, one on the tenth day from pneumonia following whooping cough and the other on the third day from

TABLE 1.—*Patients Apparently Moribund Who Were Excluded from the Series But Treated with Sulfapyridine*

Patient	Age, Mo.	Amount of Drug Received	Result
K. C.	3½	22½ gr. (1.45 Gm.)	Died
H. C.	2	5½ gr. (0.35 Gm.)	Died
M. M.	7	7½ gr. (0.48 Gm.)	Died
G. M.	1¾	75 gr. (4.85 Gm.)	Recovered
A. C.	1½	60 gr. (3.88 Gm.)	Recovered

lobar pneumonia of type XIV. While no clinical evidence of meningitis was present in the latter patient, a lumbar tap performed shortly before death revealed a mild increase in the number of cells and a few pneumococci (type XIV). One child with a single lobe affected spent eleven days in the control group and became more and more ill. Sulfapyridine was given to this child, and a prompt crisis and recovery ensued.

The 5 patients not included in these groups were those considered moribund on admission. They showed definite evidence of pneumonia but were not examined roentgenologically, as they were immediately placed in oxygen tents. Three of these infants died, each having received but a small amount of the drug, the actual retention of which is to be questioned. Two infants equally ill recovered (table 1).

The free sulfapyridine content of the blood serum was determined in 10 children, all of whom had been given the full dose for two days. Table 2 shows these levels. Because of the variability in the levels it was felt that this was not a particularly useful test. The patients with levels below 2 mg. per hundred cubic centimeters made as prompt recoveries as those with much higher levels.

In the present series no toxic effects on the kidneys were observed by gross inspection of the urine or by routine urinalysis. In other patients treated with this drug we have twice observed gross hematuria, which disappeared when the drug was discontinued.

Table 3 shows 7 patients in the treated group in whom significant changes in the total and differential white cell count were seen. In

TABLE 2.—*Determinations of Free Sulfapyridine in Specimens of Blood Taken After Administration of 1.5 Grains (0.09 Gm.) Per Pound of Body Weight for Forty-Eight Hours*

Patient	Age, Yr.	Level of Sulfapyridine, Mg. per 100 Cc.
L. Y.	5	3.6
O. P.	2½	4.4
L. deV.	4	5.0
R. B.	10	11.0
V. B.	2½	6.4
H. B.	10	1.35
L. S.	8	4.2
M. K.	2	5.6
R. deL.	6	12.0
T. O.	2½	1.2

TABLE 3.—*Significant Decreases of Polymorphonuclear Cells During Treatment with Sulfapyridine*

		Original Count			Later Count	
Patient	Age	No. of White Blood Cells	Polymorphonuclears, %	Days of Treatment	No. of White Blood Cells	Polymorphonuclears, %
N. B.	2½ yr.	4,500	61	3	4,700	37
G. E.	3 yr.	33,000	86	4	8,000	39
R. M.	9 mo.	10,750	66	4	5,250	14
R. R.	2 yr.	22,700	82	3	6,100	60
M. K.	2 yr.	14,700	69	2	15,400	37
R. P.	14 mo.	7,100	73	2	5,250	33
T. O.	2 yr.	12,700	85	2	4,100	12

only 2 of these was the number of granulocytes reduced enough to cause concern. It has been the policy during this study to stop giving the drug if the total leukocyte count fell to 5,000 or the granulocyte percentage below 35. In these 2 patients the granulocytopenia disappeared soon after the administration of the drug was stopped. No such effects were noted in any of the control subjects, for whom repeated blood counts were made.

Table 4 shows the only case in which a significant hemolytic effect was seen. The rapid fall in hemoglobin stopped when the use of the

drug was discontinued, and a rise began before transfusions were given. The child made a good recovery.

Vomiting was a troublesome symptom. It was often so severe at the time of admission that it was difficult to ascribe it entirely to the drug. However, it occurred in almost every case. The nursing staff felt that it was more troublesome in older children than in infants. They also felt that while the first few doses of the drug were often vomited, the patients acquired a tolerance to it. The vomiting often occurred immediately after the drug was taken and sometimes not until

TABLE 4.—*Patient (R. B., 2½ Years of Age) Showing Significant Fall in Hemoglobin and in Number of Erythrocytes After the Administration of Sulfapyridine*

Date	Amount of Hemoglobin, Gm.	Number of Red Blood Cells	Treatment
March 21	9.5	4,200,000	Drug started
22	8.5	3,850,000	
23	7.5	3,850,000	
25	6.0	2,690,000	Drug stopped
27	6.8	2,940,000	
29	7.0	3,520,000	Transfusion
30	...	.....	Transfusion
April 1	9.5	3,580,000	

TABLE 5.—*Vomiting Caused by Sulfapyridine*

Degree	Number of Cases
Severe enough to necessitate withdrawal	2
Rather severe	5
Moderate	10
Slight or none	41

a number of doses had been taken. As will be seen in table 5, vomiting while troublesome, was responsible for cessation of treatment in only 2 cases.

Otitis media was the only important complication. It occurred in 18 of the 58 patients treated with sulfapyridine and in 24 of the 56 controls. No operations on the mastoid were necessary in either group.

SUMMARY

Fifty-eight children and infants with pneumonia were treated with sulfapyridine. There was usually a prompt, serum-like effect in reducing temperature. Only 10 of these patients had fever after forty-eight hours. With the fall of temperature most of the patients became free of toxic symptoms and dyspnea.

As contrasted with untreated patients in a similar group, the febrile course was materially shortened; the febrile course of the treated patients averaged four and ninety-four hundredths days, and that of the controls averaged seven and thirty-nine hundredths days.

No deaths occurred in the adequately treated patients. Two deaths occurred in the control group. Of 5 moribund infants given sulfapyridine, 3 died and 2, who retained adequate amounts, recovered.

Vomiting was the principal toxic symptom of the drug. Other reactions were few, not serious and more than compensated for by the beneficial effects described.

FOCAL EPILEPTOGENIC LESIONS OF BIRTH AND INFANCY

WITH REPORT OF EIGHT CASES

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There is a group of epileptic patients whose history points to a cerebral lesion at the time of birth or during some febrile illness of infancy. The nature of these lesions which produce late habitual epilepsy has received scant attention up to the present. On the other hand, traumatic and ischemic cerebral injury has been studied exhaustively in autopsy series and the relation of such injury to cerebral diplegia has been a subject of discussion for many years.

REVIEW OF THE LITERATURE

In 1862, William Little [1] published a description of the diplegia or bilateral paralysis which he attributed almost wholly to asphyxia of the brain resulting from an accident of birth. He reported postmortem observations in only 2 cases. In one there had been gross intracranial bleeding; in the other, only congestion of the whole brain.

In subsequent years there has been much discussion of the relation of spastic diplegia (Little's disease) to birth injury and intracranial hemorrhage. Sigmund Freud [2] early turned his attention to this subject (1897), stating that he could find no evidence that diplegia was due to injury at birth. But he made a distinction between diplegia, which he considered to be due to a degenerative cerebral condition, and double hemiplegia, which he ascribed to gross intracranial bleeding. James Collier, in 1899 [3] and again in 1924,[4] likewise maintained that diplegia

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1. Little, W. J.: On the Influence of Abnormal Parturition, Difficult Labours, Premature Birth, and Asphyxia Neonatorum, on the Mental and Physical Condition of the Child, Especially in Relation to Deformities, Tr. Obst. Soc., London **3**:293, 1862.

2. Freud, S.: Die infantile Cerebrallähmung, Vienna, A. Hölder, 1897.

3. Collier, J.: Cerebral Diplegia, Brain **22**:373, 1899.

4. Collier, J.: The Pathogenesis of Cerebral Diplegia, Brain **47**:1, 1924.

was due to neuronal cerebral degeneration and not to hemorrhage. Medical literature [5] has contained numerous studies of the causes of death at birth and shortly afterward, which were well summarized by Ford.[6] It is evident that cerebral compression, produced by subdural hemorrhage, and cerebral ischemia, due to that and other causes, are of primary importance. Tears of the dural sinuses and tributary veins resulting from head molding are the most important causes of extensive intracranial bleeding (Capon [5c] Beneke,[5b] Seitz [5a] and Holland.[5e]) But generalized asphyxia must affect the brain also, and Craig [5d] pointed out that among those infants who died at birth there were numerous evidences of severe asphyxia to be found in other organs quite independent of the intracranial findings. Rydberg [5f] concluded after an exhaustive study that actual softening of areas of the brain could be produced by cerebral compression and supratentorial hemorrhage.

Those children who have received milder injuries and therefore survive have been given less attention, and few autopsies of such persons are available. Hannes [5g] attempted a follow-up study of children who had been subjected to asphyxia and compared them with a group whose birth was said to have been associated with trauma. There seemed to be about an equal number of mentally defective children in each group, and only 3 of the 39 children studied had become epileptic.

That there is a relation between epilepsy and birth injury has been obvious to all clinicians. But Ehrenfest in his monograph on birth injuries [7] reached no conclusion as to the nature of this relation, and

5. (*a*) Seitz, L.: Ueber Hirndrucksymptome bei Neugeborenen in Folge intracranieller Blutungen und mechanischer Hirninsulte, Arch. f. Gynäk. **82**:529, 1907. (*b*) Beneke: Ueber Tentoriumzerreissungen bei der Geburt, sowie die Bedeutung der Duraspannung für chronische Gehirnerkrankungen, München. med. Wchnschr. **57**:2125, 1910. (*c*) Capon, N. B.: Intracranial Traumata in the Newborn, J. Obst. & Gynaec. Brit. Emp. **29**:572, 1922. (*d*) Craig, W. S.: Intracranial Haemorrhage in the Newborn, Arch. Dis. Childhood **13**:89, 1938. (*e*) Holland, E.: Cranial Stress in the Foetus During Labour and Effects of Excessive Stress on the Intracranial Contents, J. Obst. & Gynaec. Brit. Emp. **29**:549, 1922. (*f*) Rydberg, E.: Cerebral Injury in Newborn Children Consequent on Birth Trauma, with an Inquiry into the Normal and Pathological Anatomy of the Neuroglia, Acta path. et microbiol. Scandinav., 1932, supp. 10, p. 1. (*g*) Hannes, W.: Zur Frage der Beziehungen zwischen asphyktischer und schwerer Geburt und nachhältigen psychischen und nervösen Störungen, Ztschr. f. Geburtsh. u. Gynäk. **68**:689, 1911.

6. Ford, F. R.: Cerebral Birth Injuries and Their Results, Medicine **5**:121, 1926.

7. Ehrenfest, H.: Birth Injuries of Child, New York, D. Appleton and Company, 1922.

Lennox and Cobb [8] in their book on epilepsy ignored birth injury almost completely. Ford [6] reported 8 cases of focal epilepsy associated with congenital hemiplegias or monoplegias. He concluded that in about one third of all children with spastic paralysis due to birth injury, focal or generalized convulsions develop. He also stated that his own observations and other reports indicated that epilepsy in approximately 2 to 3 per cent of all cases is related to birth injury. Our experience now indicates that this percentage should be considerably higher.

CASES ANALYZED

This communication is based on a series of cases of habitual epilepsy in which the cerebral lesion dates back to birth or infancy. A general report of the nature of these early lesions is made here. More detailed histologic study of such cases as well as examples of cerebral injury later in life will be reported shortly by Penfield and Humphreys. All of the patients here reported on have had craniotomy and radical excision of epileptogenic foci, but they are selected for use here from a larger number of such examples only in order to throw light on the nature of these early lesions and on the fate of the brain which contains them, and not primarily for an assessment of the value of surgical therapy, a report of which has been made previously (Penfield [9]).

The lesions include areas (1) of focal atrophy and of focal microgyria due to ischemia, (2) of meningocerebral cicatrix due to depressed fracture of the skull or to infantile meningitis and (3) of focal cerebral thrombosis secondary to arterial occlusion.

REPORT OF CASES

CASE 1.—*Cerebral atrophy and meningeal adhesions secondary to infantile meningitis.*

J. D., a 30 year old man employed as a drug clerk, had a normal birth but at the age of 6 months had a febrile illness which resulted in partial paralysis of the left upper and lower extremities. When he was 16 years old, epileptiform seizures appeared, characterized by a sensation of dizziness followed by twitching of the left side of the face, turning of the head to the left and clonic movements of the left arm and leg. The attacks often became generalized.

Physical examination showed an intelligent young man who had a spastic left hemiparesis, moderate atrophy of the left extremities and defective appreciation of cortical sensation on the left side. Encephalography showed the right lateral ventricle to be larger than the left, with a superficial cyst in the right frontal

8. Lennox, W. G., and Cobb, S.: Epilepsy, Harvard Medicine Monographs, Baltimore, Williams & Wilkins Company, 1928, vol. 14.

9. Penfield, W.: Epilepsy and Surgical Therapy, Arch. Neurol. & Psychiat. **36**:449 (Sept.) 1936.

area and deviation of the septum pellucidum to the right. Lateral views demonstrated a superficial cystic area in the frontal region and another in the parietal region (fig. 1).

Osteoplastic craniotomy on the right side was carried out. The dura was densely adherent to the pia and could be lifted only by sharp dissection, especially

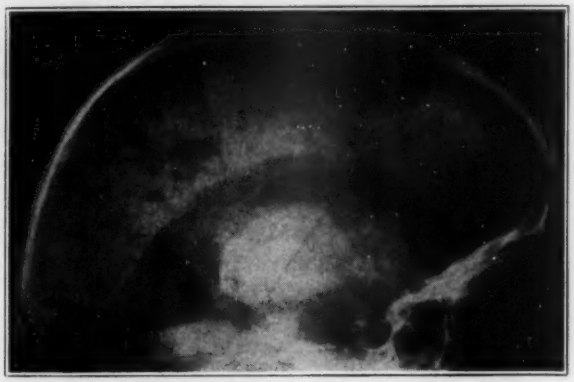

Fig. 1 (case 1).—Pneumoencephalogram, lateral view, showing outline of the lateral ventricle. Oxygen is also seen in the two superficial cysts in the parietal and the frontal region.

Fig. 2 (case 1).—Photograph of the brain at operation after the reflection of dura. The two areas indicated in the encephalogram are plainly shown.

in the posterior portion. These adhesions contained blood vessels passing from the dura down into the pia and in our opinion could have been produced only by an active inflammatory process. There was a considerable amount of convolutional atrophy. The pia was thickened everywhere, and the superficial vessels were tortuous. Anteriorly in the frontal lobe there were a cyst and some increase in the atrophy (fig. 2). Posteriorly and below there was a large focal lesion (fig. 2,

at instrument point) where fluid had collected, and beneath the fluid there was yellowish glial tissue which extended through to the wall of the underlying ventricle. This circumscribed area was adjacent to the motor gyrus, as was proved by stimulation, and the motor gyrus was actually posterior to its expected position within the skull. This posterior lesion was removed without any disability being produced, and the attacks were decreased in number but not abolished. The failure to secure a better result may have been due to the diffuseness of the abnormality.

Comment.—The febrile illness reported at the age of 6 months must have been severe meningitis which produced dense meningeal adhesions, moderate diffuse atrophy of the brain and focal destruction, especially in the posterior part of the right hemisphere. The destruction must have been due to interference with cortical circulation at the time of infection. This focal destruction was complete, leaving only gelatinoid

Fig. 3 (case 2).—Photograph at operation. The cicatricial lesion is seen to be just posterior to the central fissure. The threads indicate the extent of the removal posteriorly; the removal anteriorly was carried out by dissection.

glial tissue with no preservation of normal cerebral structure. The total volume of the right hemisphere was reduced, which explains the fact that the septum pellucidum was nearer to the right side. The Rolandic cortex had migrated posteriorly, owing to the destruction of tissue behind it.

CASE 2.—*Meningocerebral cicatrix secondary to depressed fracture of skull at birth.*

D. D. was a girl of 14 who was referred to us by Dr. Pincock, of Brandon, Manitoba, Canada, because of epileptic seizures. Her birth had been induced at 8 months because her mother had pneumonia. Delivery was carried out by forceps, and there was obvious depression of the right side of the skull. The child cried lustily but had to be fed with a dropper during the first five days of life. On the fourth day there began a series of convulsions which lasted for

ten hours, and again on the fifth day a similar series occurred. Weakness of the left arm and leg was observed immediately after the convulsions. Following the seizures there was jaundice, which lasted two months. The child talked at 1 year of age and walked at 3 years. Mental development was normal.

At the age of 11 the girl began to have left-sided seizures, which occurred as often as two or three times daily. These seizures often came directly after she was startled by a sudden noise. In each attack she threw the left arm up and became conscious of a peculiar sensation in the left wrist. There were then flexion of the wrist, extension of the fingers, turning of the head and eyes to the left, and clonic movements of the left arm, left leg and left side of the face. There was no loss of consciousness.

On physical examination at the age of 14, the patient was seen to be normally developed except that her left hand was smaller than her right and the left side of her chest was a little smaller than the right side. There were partial left homonymous hemianopia and left external strabismus. Encephalography showed the septum pellucidum to be nearer the right side than the left. The posterior part of the lateral ventricle (portion 4) and the inferior horn (portion 6) on the right side were enormously enlarged.

Operation was carried out with the area under local anesthesia. There was a discrete scar in the brain, situated in the postcentral gyrus (fig. 3). It touched the precentral gyrus only at the level of the hand area. The bone over the scar was pitted. The dura was deficient over the pitted areas and strongly adherent to the scar elsewhere. Electrical stimulation produced motor responses in shoulder, arm or hand from the gyrus just anterior to the scar, as indicated by the response tickets from 1 to A in figure 3. Convulsive seizures were produced by stimulation at the site of each of the tickets marked # 1, # 2, # 3, # 4 and X.

Excision of the scar up to the edge of the motor gyrus was carried out. The operative result was good as far as seizures are concerned, for she has been free from attacks up to the present, a year and a half since the operation. However, there has been a definite increase in the disability of the left arm, owing, no doubt, to the proximity of removal to the motor gyrus and perhaps the underlying pyramidal tract.

Comment.—This was a typical example of the result of depressed fracture of the skull and cerebral laceration due to forceps pressure at birth. The marked cerebral atrophy about the region doubtless resulted from the direct injury and from the disturbance of circulation associated with it. There were no narrow gyri.

CASE 3.—*Focal microgyria secondary to ischemia of birth.*

Because of epileptiform seizures at the age of 16, G. A., a young girl, was referred to us by Drs. Foster Kennedy and Jefferson Browder, of New York city. At the time of the patient's birth her parents were living in Japan. Her mother was given twilight sleep, and the labor was terminated after thirty-six hours by the application of forceps. The cord was said to be about the neck, and the infant was large, weighing 9½ pounds (4,309 Gm.). There was much initial cyanosis, and there was difficulty in making the child breathe.

After this the infant seemed to be well enough until about two weeks later, when she began to have generalized convulsions. These lasted from two to three days. The child was placed in an oxygen tent, and the physician told the parents he had little hope of her recovery. However, she did recover and seemed to develop normally, except that she was slow in beginning to walk and that from the first

she seemed to use the left arm and leg less well than the right. In time she became a normal-looking child who showed no obvious disability, progressed in school and played a good game of tennis.

At the age of 10 years the girl began to have epileptiform seizures, which continued during the succeeding six years, until she came under our care. Attacks of three distinct types appeared at different times: (1) sensory seizures, which were characterized by an aura of tingling in the left arm and sometimes also in the left leg; (2) facial attacks, which began with an aura of sensation in the left side of the mouth and the left side of the tongue and might spread to clonic facial movements and which occurred from one to four times daily, particularly after the patient was startled, and (3) adversive attacks, which appeared later in life and were characterized by forcible turning of the head and eyes to the left. The turning of the head in the third type of attack was sometimes clonic. The

Fig. 4 (case 3).—Pneumoencephalogram taken in brow-up position, showing the septum pellucidum nearer the right than the left side. The right cranial chambers are much smaller than the left. Enlargement of the body of the right lateral ventricle is shown (portion 3).

girl said her eyes were "pulled to the left" and she could not turn them back to the right again. The attacks occasionally became generalized.

Physical examination showed an attractive, intelligent girl with a comparative decrease in the size of the left arm, left side of the thorax and left leg, a defect of appreciation of two point sensation in the left arm and leg and astereognosis in the left hand. Otherwise there was no abnormality and no evidence of a lesion of the pyramidal tract.

Encephalography (fig. 4) showed that the right hemisphere was smaller than the left, the septum pellucidum was closer to the right vault than to the left and the posterior portion of the body of the right lateral ventricle was moderately enlarged. At operation in June 1937 a large right-sided osteoplastic craniotomy was carried out under local anesthesia. There were no adhesions between the dura and the arachnoid, which indicated clearly that there had been no subdural

hemorrhage at the time of birth. There was no yellowing of the pia-arachnoid. The arachnoidea, however, was almost white in certain areas, and the subarachnoid space was a little deeper than usual (fig. 5). Corresponding with these areas of whitened arachnoid there were three distinct areas in which narrow gyri were present—frontal, upper postcentral and lower postcentral (areas *C*, *B*, and *A* in fig. 5). These thin gyri, which were made up of tough, yellowish cerebral tissue, were excised, and it was found that the upper and lower postcentral gyri were connected by a narrow submerged gyrus, most of which was removed by tunneling. The spaces from which each of these zones of microgyria was removed are shown in figure 6. There was no disability as the result of operation, and there have been no further attacks up to the present—eighteen months after operation.

Comment.—In this case it seems possible to reconstruct the elements which produced these lesions at the time of birth. The birth was of long

Fig. 5 (case 3).—Photograph of the brain at operation. There is a thickening of the arachnoid over the three areas of focal atrophy—*A*, the lower postcentral, *B*, the upper postcentral and *C*, the frontal.

duration, the umbilical cord compressed and the child large; forceps were used. This state of affairs produced direct cerebral compression and also arrest of the fetal circulation, resulting in severe cerebral ischemia. Nevertheless, the child was resuscitated, and the blood pressure rose sufficiently to restore the circulation in most parts of the brain, thus preventing their destruction. For some reason the postcentral gyrus and the isolated gyrus lying anteriorly near the frontal eye area were ischemic longer than the rest of the brain was. The ischemia of these isolated gyri was of longer duration than the contained nerve cells could endure. The neural elements in these convolutions were therefore largely destroyed, leaving their glial elements only.

This was not the result of thrombosis of a larger artery, for the distribution was not that of any one or even two arteries. Compression of the convolutions in question may have been slightly greater than that of other convolutions during the period of defective blood supply, owing to some difference in pressure mechanism, or it is possible that vascular spasm was an element in the production of greater ischemia. During operation we have seen an individual convolution become blanched as a unit and remain so for a considerable period (Penfield [10]).

This was not a case of subdural hemorrhage. There were only two small, tenuous adhesions, and there was no yellowish discoloration except of the destroyed gyri. Furthermore, as the child nursed well after the

Fig. 6 (case 3).—Photograph taken one hour later to show that the small gyri in the three zones have been removed. The tickets indicate points from which responses were obtained by electrical stimulation.

three days of convulsions, there was no continuing cerebral compression such as might have resulted from subdural clot. Also, this was not a case of intracerebral hemorrhage, for such a hemorrhage would not confine itself to individual convolutions, and the type of cerebral destruction produced would have been different. This is not a case of venous thromboses, as the cerebral veins usually drain at least two adjacent gyri, not one.

This case seems to establish clearly the fact that long-continued labor, associated with defective fetal circulation, can produce a focal

10. Penfield, W.: The Evidence for a Cerebral Vascular Mechanism in Epilepsy, Ann. Int. Med. **7**:303, 1933.

lesion within the brain as well as more diffuse cerebral destruction. The few days of convulsions which followed shortly after birth doubtless were associated with returning circulation in various parts of the brain. We have seen such a series of seizures in adults several days after ligation of a pial artery. The attacks were followed by evidence of restitution of circulation (Penfield [9]).

The encephalogram (fig. 4) showed the septum pellucidum to be nearer the right side and the whole ventricular system to have shifted a little from left to right. The ventricles were moderately enlarged, especially the posterior portion of the body of the right lateral ventricle. This doubtless corresponded with the atrophic postcentral convolution.

When focal areas of brain have been destroyed at birth there occurs during subsequent growth of the brain a rearrangement, other portions of the brain being crowded into the space left by the atrophy of the injured portion. The result is that surprisingly little asymmetry or abnormality may appear in the ventricular outline because of the fact that the head grows only in response to the growth of the brain. The brain, convoluted as it is, therefore rearranges itself by means of its pressure against the skull on the outside and the pressure on it from the inside of the ventricular fluid system. The total volume of the right hemisphere in this case was obviously less than the total volume of the left, but the general shape was the same.

Clinically the patient showed only a defect in cortical sensation resulting from the destruction of the postcentral gyrus but no motor difficulty and no evidence of a pyramidal lesion, a further testimony to the discreteness of the destruction. The hemiatrophy of the left side of the body results invariably from postcentral gyrus destruction, as shown by Penfield and Robertson,[11] and not from destruction in other areas of the brain. This was seen in case 1 as well.

CASE 4.—*Cerebral atrophy and focal microgyria secondary to subdural hemorrhage and focal ischemia at birth.*

W. K., a boy of 18 years, was referred to us by Dr. Stanley Cobb, of Boston, in March 1936. The mother's labor had presented difficulties. To quote from the report of the obstetrician: "This was a breech presentation, left sacroanterior position, and the delivery was not difficult. The child was very much asphyxiated and required prolonged resuscitation. On the second day there was marked evidence of intracranial hemorrhage, i. e., twitching without actual convulsions and a tense anterior fontanel. These symptoms gradually subsided, and the child did well thereafter." The boy is said to have been somewhat backward at the age of 5, and at the age of 8 he had an operation for torticollis.

Recurring epileptic seizures began at the age of 15. A typical attack was ushered in by a "rising" sensation in the epigastrium associated with thirst. This

11. Penfield, W., and Robertson, J. S. M.: Growth Asymmetry in Relation to Cicatrical Cortical Lesions, to be published.

was followed by a cry, turning of the head to the left, twitching of the mouth to the left and unconsciousness. After an attack he was dazed and could not speak.

On arrival at the Montreal Neurological Institute the boy was found to be well developed and muscular. His head was small and a little flattened on the right side. Results of neurologic examination were negative and mentally he seemed to be within normal limits. A simple roentgenogram showed the right side of the cranial cavity to be small and the falx nearer to the right side than to the left (fig. 7). The right side of the skull was more dense than the left. Encephalography showed that the whole right hemisphere was smaller than the left, with the septum pellucidum displaced to the right. The ventricles were slightly large for a boy of his age. The posterior end of the lateral ventricle (portion 4) was enlarged on the right, and the inferior horn on the right was enormously enlarged. It was

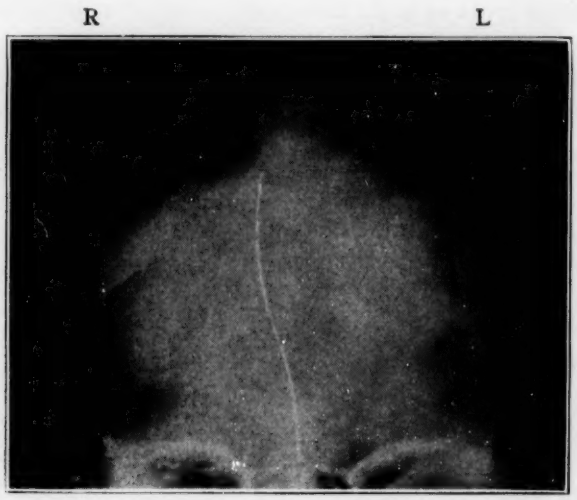

Fig. 7 (case 4).—Anteroposterior view of the skull, showing less development of cranial chamber on the right side. Calcification of the falx indicates its position.

evident, therefore that the right hemisphere occupied less space than the left and that there was comparative atrophy of the right temporal lobe.

At operation a right osteoplastic craniotomy was carried out. There were marked adhesions everywhere beneath the dura, rather more marked in the posterior parietal region. But in these adhesions there were no vessels crossing between the pia and the dura. The adhesions were fine and filamentous but numerous. Most of them could be separated by blunt dissection, but scissors had to be used in certain areas.

The region of the brain around the central fissure of Rolando appeared essentially normal. There was marked atrophy of the convolutions of the temporal lobe, that is, enlargement of the intergyral sulci but with little narrowing. This was perhaps most noticeable in the lower temporal region, where there was intense gliosis, to judge by the hard consistency of the cerebral tissue there. In the posterior parietal region there was a discrete area in which the convolutions were decreased to about one-third their normal size (fig. 8).

About the periphery of this parietal area of microgyria the aura of his attacks, namely, "a rising sensation in the chest," was produced at points *1, 2, C, B* and *D* in figure 8. This entire area was excised as shown by the broken line in figure 8. The excision opened the posterior end of the ventricle. In the two years and a half that has followed operation he has had an occasional "rising sensation" but no convulsions and has carried on satisfactorily with his college work.

Comment.—In retrospect two pathologic conditions may be said to have operated in the production of the abnormalities found here. The first factor was a subdural hemorrhage which occurred at birth. The evidence of this was the adhesion which was found between the arachnoidea and the dura. This was typically made up of small threads, which allow for some movement of the brain. These threads were of

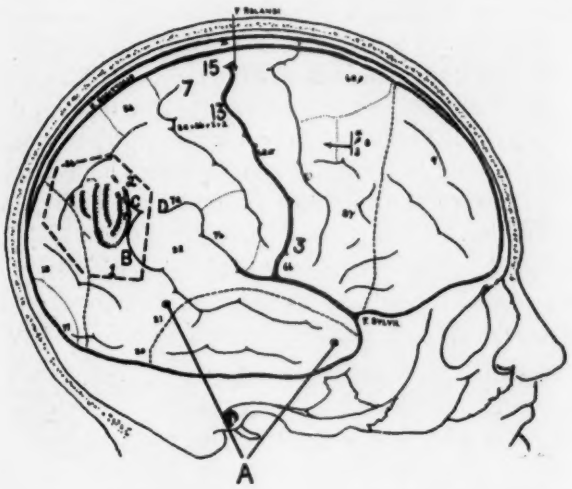

Fig. 8 (case 4).—Diagram to indicate the site of focal microgyria. *A* indicates the cortex in which the convolutions were hard and the intergyral fissures wide beneath old subdural hematoma. The broken line surrounds the area of cortical atrophy, microgyria due to focal ischemia. Stimulation responses were as follows: *3,* numbness of the left side of the tongue; *15,* numbness of the lower part of the left leg; *13,* numbness in arm and hand; *7,* feeling in the left side of the stomach "that is not like my attack"; *1, 2, C, B* and *D,* a "rising feeling" in the midthorax somewhat like the patient's habitual aura.

varying thickness. If there had been a depressed fracture, another type of adhesion would have appeared which would have been dense and would not have elongated and in which there would have been blood vessels passing from the dura into the brain, as in case 2. These tenuous adhesions, however numerous they may be, do not as a rule provide for transsubdural vascularization.

The marked atrophy of the temporal lobe, without microgyria, suggests that there was a large enough subdural hematoma to produce

intracranial pressure continuing over the period of greatest growth of the head, i. e., the first two years. With absorption of the clot, the inferior horn of the ventricle enlarged to fill in the cranial space. This injury of the temporal lobe could doubtless have been prevented by subdural drainage of the blood clot after birth. This is atrophy of brain with atrophy of convolutions but without pushing together of the convolutions such as occurred in the parietal region.

On the other hand, the rather focal area of small gyri in the parietal lobe, the histology of which has been carefully studied, indicates that in that particular portion another pathologic factor is to be considered. Here the circulation was cut down acutely for a long enough period during birth so that the nerve cells could not recover or could only partially recover, and the convolutions did not grow. On the contrary, they shrank and were pushed together by the growth of neighboring convolutions. The fact that the falx is nearer the right side than the left shows that the growth of the brain on the left was greater than on the right and that the skull was pushed out normally during the growth period on that side. There was no cyst formation in the brain and no evidence of either an intracerebral hemorrhage or occlusion of any particularly large cerebral artery.

It is interesting to observe that the initiation of the seizures seems to have been related to the area of microgyria rather than to the area in which the subdural hematoma left its principal telltale.

CASE 5.—*Moderately focal atrophy due to ischemia at birth.*

M. D. was a girl of 16 who was referred to us by Dr. J. MacDonald, of Indianapolis, because of focal epileptic seizures. She had been one of twins; the other was born dead, the labor having been difficult and forceps used. A good deal of work was required to initiate respiration in her case, and during the first three days of life she had generalized convulsions. There seems to have been no evidence of increased intracranial pressure, and the child took her feedings and developed normally during infancy.

At the age of 3 years, after a severe cold, the patient had a generalized seizure. At the age of 5 there was a similar attack, and at 9 years she had the first of her typical convulsive seizures. These seizures were habitually ushered in by sensation in the mouth and on the left side of her tongue. This was followed by twitching of the mouth and inability to speak, although consciousness was retained.

On the patient's admission to the hospital, in 1933, the encephalogram showed moderate enlargement of the right ventricle and greater enlargement of the left ventricle. A large frontoparietal osteoplastic craniotomy on the right side was carried out. There was evidence of rather diffuse change in the hemisphere. Some of the convolutions were small, but there was no focal area to be made out objectively. On the basis of stimulation the face area was removed on the right side. It was impossible to remove all abnormal tissue, obviously. Since operation in May 1933 the patient has had only 4 attacks, two in April 1936 and two in October 1937.

Comment.—It seems fair to interpret this case as follows: There was marked asphyxia at birth, and the brain suffered from ischemia, which

doubtless involved the right hemisphere more than the left. During the first few days, the patient had a series of seizures because of this ischemia. There resulted a diffuse lesion of the cortex from which the patient did not wholly recover and which later was responsible for her habitual seizures and for the seizures which began at the time of her early febrile attack.

CASE 6.—*Focal microgyria due to ischemia at birth.*

N. I., a boy of 16 referred to us by Dr. W. Leslie, of Winnipeg, Manitoba, Canada, was admitted because of convulsive seizures; he was a twin. At birth

Fig. 9 (case 6).—Pneumoencephalogram shows the left cranial chamber to be smaller than the right, but the anterior end of the ventricle is about equal in size.

he is said to have been delivered easily, but he was followed by a twin brother who was dead, and there was reason to suspect that he too had been injured. Infantile development was slow; he nursed poorly and was underweight. He walked at 1½ years of age and talked at 2 years.

At 18 months the boy had an intestinal disturbance, a high fever and several convulsions during one day. He was well after this until the age of 7 years, when convulsive seizures reappeared; except for a free interval between the ages of 10 and 13, these became regularly recurrent up to the time when we saw him. The habitual attacks began with an aura of peculiar sensation in the right arm. This was followed by involuntary flexion of the right arm. The attack might stop there or might proceed to generalized convulsive movements. He was a

strong, well developed boy who had progressed satisfactorily in school, although his power of concentration was said to be defective. His deep reflexes were somewhat decreased but symmetric. Otherwise examination revealed nothing abnormal.

Cerebral pneumography showed the third ventricle and septum pellucidum to be a little nearer the left side than the right and the left cranial chamber to be a little smaller than the right, as shown by the position of the falx. Encephalograms in other positions showed that there was enlargement of portion 4 of the left lateral ventricle (fig. 9).

A large osteoplastic craniotomy on the left side was carried out, and electrical exploration showed that the central fissure was proportionally much more posterior than was expected, as indicated by the line of dots in figure 10. Just posterior to the postcentral gyrus and situated largely within the longitudinal fissure was an area (fig. 10) where the gyri were crowded together and of a diameter not more than one third that of the normal-appearing gyri elsewhere. This area of small packed gyri was excised radically. The boy recovered from operation without

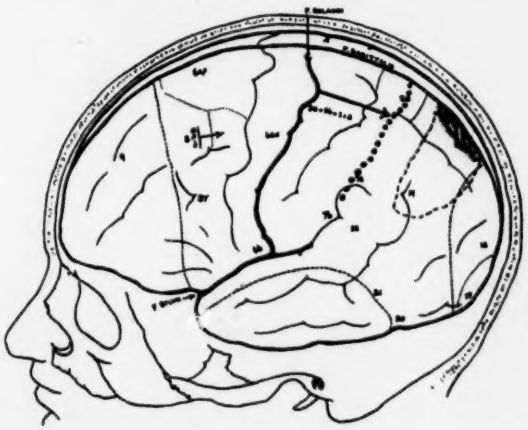

Fig. 10 (case 6).—Diagram to show the position of the area of focal microgyria and the resultant posterior migration of the central fissure to the line of dots.

defect and up to the present time—twelve months after operation—there have been no further seizures.

Comment.—This boy had no subdural hemorrhage at birth because there were no telltale subdural adhesions. But he did have mechanical compression of the brain which was sufficiently focal to produce ischemia of the convolutions of one area. Thrombosis of a cerebral vein might have been an element in this case because of the position, but it seems evident that ischemia at birth largely destroyed the neural elements in this posterior central area so that the rest of the left hemisphere crowded toward that region during growth of the skull, producing the astonishing posterior displacement of the rolandic fissure toward the area in question. The small size of the left cranial chamber is obviously the result of the decrease in total hemisphere.

CASE 7.—*Focal cerebral atrophy secondary to arterial occlusion during infantile disease.*

L. B., a man 22 years of age, was referred to us by Dr. A. Wheaton, of Sussex, New Brunswick, Canada, because of jacksonian epilepsy. The history of the birth and early months of this patient was normal. At the age of 9 months he had had pneumonia, which was followed by a hemiplegia of the right side. Since that time he had been partially paralyzed on the right side.

Epileptiform seizures began at the age of 16 years and occurred about once a month up to the time of admission. The seizures were right sided and were

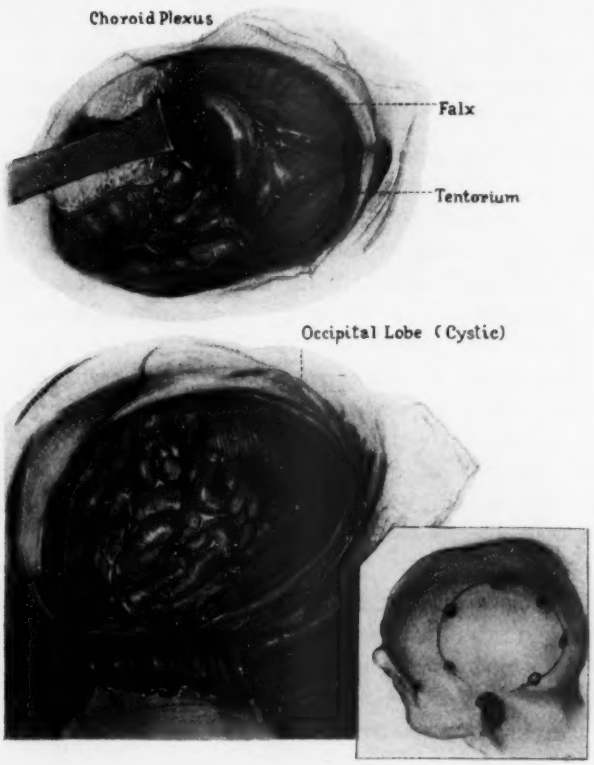

Fig. 11 (case 7).—Drawings at operation to show the left occipital lobe converted into a membranous sac containing fluid. After amputation the falx tentorium and the choroid plexus within the ventricles are seen.

ushered in by a sensory aura, either a feeling down the right side of the body or, less often, a sensation of choking. On examination he was found to have a right homonymous hemianopia and right hemiparesis. The encephalograms showed definite shift of the whole ventricular system from right to left (approximately 2 cm.). The left lateral ventricle was enormously enlarged in the posterior half, with thinning of the brain tissue. The right ventricle was not unusual.

At operation, in December 1931, a posterior osteoplastic craniotomy was carried out on the left side. The dura was reflected freely from the brain, as there were

no adhesions in the subdural space. The posterior end of the occipital lobe was found to be converted into a membranous sac filled with cerebrospinal fluid (fig. 11, lower sketch). The line of demarcation between this sac and the brain was sharp, particularly so on the mesial side. The motor gyrus seemed to be of good color, but the neighboring gyri back of it were somewhat brown, although nearly normal in outline. Posterior to this there were one or two extremely narrow gyri before the whole brain was changed into a membrane. The focus from which the patient's typical epileptiform aura could be produced by electrical stimulation was in the lower part of the hemisphere anterior to the membranous sac at points 10 and 6 (fig. 11).

Complete excision was carried out, the line of removal being carried up to what seemed to be normal brain (upper sketch, fig. 11). The result was freedom from seizures for only one and one-half years, after which time there have been two or three attacks yearly up to the present. It is possible that wider excision in the vicinity of the aura focus would have given permanent freedom from attacks.

Comment.—In retrospect it may be seen that this is a case of occlusion of the posterior cerebral artery and possibly some branches of the middle cerebral artery on the left side. Occlusion evidently took place during the febrile illness at the age of 9 months. The fact that no adhesions were found shows that there had been no hemorrhage, as in case 2, and no meningitis, as in case 1. The brown discoloration of the posterior end of the relatively normal brain suggests that there had occurred perivascular diapedesis of red blood cells within the zone of brain that separated that portion which became completely ischemic, and therefore was completely destroyed, and the normal brain, which was not altered. Slowing of circulation results regularly in perivascular diapedesis, whereas complete cessation has no such effect. The pigment of the red cells is regularly converted into a brown stain which is visible years afterward.

Such a series of events as is described in this case has commonly been diagnosed in the literature as infantile encephalitis. It seems more likely to us that in infancy acute dehydration during a fever, regardless of the cause of the fever, may result in thickening of the circulating blood and consequently spontaneous thrombosis of one or more cerebral arteries.

CASE 8.—*Focal cerebral atrophy due to prenatal arterial occlusion.*

A. M., a woman aged 25, was referred to us by Dr. R. H. McGibbon, of Montreal, Canada, because of hemiplegia and jacksonian epilepsy. There was no history of injury at birth. The position had been transverse, and some force was used, but no instruments. Although she was rather blue when delivered, she breathed easily and fed well. She was not drowsy, and there were no convulsions. One week after birth the mother states that it was first observed that the child's right elbow and wrist were held in a flexed position and that there was apparent paresis of that limb. At the age of 2 months weakness of the right leg was noted, and the extremities on the right were obviously smaller than those on the left.

On admission to the Montreal Neurological Institute the patient was found to have slight mental retardation. The right arm and leg were smaller than the

left. She had a right hemiplegia which was not complete. She could walk well, although the right leg was spastic. The right upper extremity was kept flexed in a tonic manner, but she was capable of making crude voluntary movements.

Roentgenograms showed the skull to be asymmetric, the left side being much flatter than the right. Encephalograms showed the whole ventricular system to be nearer the left vault than the right. There was enormous dilatation of the left lateral ventricle, involving portions 2, 3, 4 and most of portion 6. The left hemisphere was thus much reduced in size, while its ventricular spaces were much increased in size, especially posteriorly, and yet the general ventricular form was preserved.

The seizures of which she complained began with a peculiar sensation in the paretic right hand, which she described as "pins and needles." This sensation traveled up the right arm and down the right side into the leg, and then the patient lost consciousness. At this time violent shaking of the right arm and leg occurred,

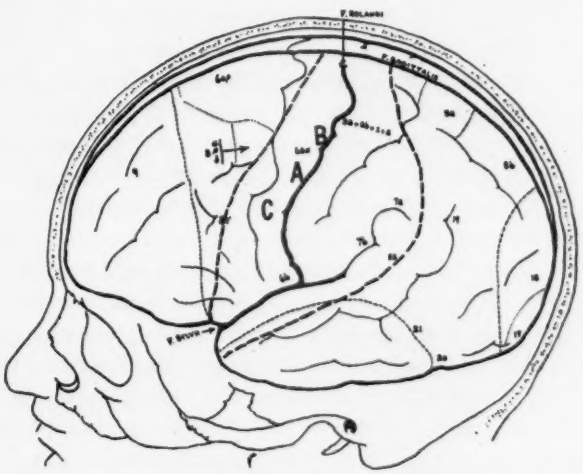

Fig. 12 (case 8).—Outline to show extent of cyst and operative removal, as indicated by broken line. (For responses *C*, *A* and *B* see text.)

and the head was turned to the right side. The attacks occurred once or twice a week as a rule, although she had had free periods of from one to eight months.

In February 1937, osteoplastic craniotomy on the left side was carried out with the patient under anesthesia induced with avertin with amylene hydrate and an extremely small dose of ether. There were no adhesions between the dura and the brain aside from pacchionian granulations, which were found farther from the midline than usual. There was nothing to suggest a previous hemorrhage. The brain itself appeared normal anteriorly and posteriorly, but it was replaced in the region where the fissure of Sylvius should have been by a wide gutter of altered tissue containing one small cyst. This altered tissue extended upward and backward from the position of this fissure to the falx (fig. 12). Thus the abnormal zone extended from the middle fossa upward to the longitudinal sinus. Outside this zone the gyri appeared normal.

In the side of the upward extension of the cerebral lesion there were narrow abnormal gyri which were proved by stimulation to be the rolandic gyri. Electrical

stimulation of that area gave closure of the mouth and swallowing from point *A* (fig. 12), inward rotation of wrist from point *B* and closure of the mouth from point *C*. Stimulation elsewhere was without result.

The cicatricial tissue was removed entirely with deep brain sutures and blunt dissection. It became evident during the extirpation that there was no middle cerebral artery, although the scar itself had pulsated actively. The excision was carried upward to include the convolutions on either side of the fissure of Rolando as far as the falx itself (broken line in fig. 12).

After operation there was no alteration whatever in the function of the paretic arm and leg and no alteration in speech. The postoperative course has been satisfactory, inasmuch as the attacks have ceased completely for two years up to the present time and the patient is much more alert mentally, owing, no doubt, to the cessation of seizures.

Comment.—There was no extracerebral hemorrhage at birth in this case, as shown by the absence of adhesions between dura and pia, and there was no intracerebral birth hemorrhage, as may be concluded from the fact that the baby breathed and nursed well from the beginning and also from the absence of brown pigment in the lesion. There was complete destruction of a large area of brain, due evidently to complete ischemia. The area corresponds with the location of the middle cerebral artery, and the destruction was evidently due to occlusion of this artery. It seems probable that this occlusion occurred some time before birth, because of two facts: (1) The arm and leg were held in a flexed position at least as early as the first week after birth instead of being flaccid, and (2) the right arm and leg were noted to be comparatively small at the age of 2 months. There is no clue from the history as to the cause of thrombosis of that artery. Enough representation of the right arm remained in the left hemisphere to produce the recurring epileptic seizures, and there was slight response to stimulation; and yet complete extirpation did not decrease function in that limb or in the face and leg. This argues for ipsilateral control—most in the face and leg, less in the arm—and suggests that the only influence the contralateral cerebral cortex exerted resulted in epileptic seizures.

GENERAL OBSERVATIONS

In conclusion, it is evident that birth may produce focal lesions of the brain in a variety of ways and with different characteristic end results. Such lesions may be difficult of detection in later years because of readjustments during the period of growth. The enlargement of the skull which is so rapid in the early years of life occurs in response to the outward thrust of the growing cerebral hemispheres. If a focal lesion occurs in this earliest period of growth, the normal convolutions which are capable of enlargement crowd toward this zone, which does not grow. The rearrangement thus produced may be sufficient to preserve the shape of the underlying ventricle to a large extent, whereas

a similar lesion later in life would produce a greater corresponding outpocketing of the ventricular wall. Consequently, decrease in the size of one cranial chamber should be recognized as consistent with the existence of a focal lesion of the brain early in life.

This displacement of structure may cause movement of gyri to a distance forward or back, as in case 6, and even from the midline outward, as shown in case 8 by the lateral placement of the pacchionian granulations and the unexpectedly lateral position of the veins, which ordinarily leave the surface of the brain at the longitudinal fissure to enter the longitudinal sinus.

Focal microgyria seems to be produced by the following mechanism: The initial injury is ischemia, produced by cranial pressure during passage of the infant through the birth canal, associated with temporary interference with fetal circulation. Nerve cells can survive complete anoxemia only a short time. It is possible, therefore, that the ischemia is severe enough in the gyri in question to result in the death of neurons and the preservation of the more resistant neuroglial cells. Thus, even if only a few ganglion cells are preserved the general structure of the gyrus is undisturbed, and the focal microgyria if uncomplicated presents no adhesions. There may be whitening of the overlying pia-arachnoid, as in case 3.

Large *vascular occlusions* early in prenatal or postnatal life produce greater ventricular distortion than do the partially destroying lesions which result in focal atrophy. Focal cortical destruction due to arterial occlusion also occurs without overlying adhesion. Such vascular occlusion may occur during the febrile illnesses of infancy without evidence of local infection. We suggest that it may be the result of extreme dehydration at such times. This may well be the explanation of the condition called encephalitis of childhood.

Occlusion of a cerebral artery evidently may occur in utero, as in case 8, in which there was no evidence of birth injury and in which flexed posture of the upper extremity was noted at the age of 1 week and smallness of the lower extremity at the age of 2 months. Arterial block produces complete destruction and disappearance of normal structure (Evans and McEachern [12]). On its border there may appear narrow, shriveled gyri which would seem to serve as epileptogenic foci. Evidently in these marginal narrowed gyri the circulation at the time of the vascular closure was reduced only enough to produce partial destruction as in the case of simple microgyria, leaving the neuroglia, the vessels and some of the ganglion cells.

12. Evans, J., and McEachern, D.: The Circulatory Changes in Cerebral Vascular Occlusion and in Cerebral Cicatrization, A. Research Nerv. & Ment. Dis., Proc. **18**:379, 1937.

Meningocerebral cicatrix is obviously the result of local laceration and produces the densest sort of adhesion. These adhesions contain anastomosing blood vessels and intermingling of connective tissue and glia. In this case also the actual origin of discharge in an epileptic seizure lies at the periphery of the area of complete destruction.

Infantile meningitis produces dense, vascularized adhesions between pia and dura, irregular thickening of leptomeninges and destruction of underlying brain, evidently by means of interference with circulation of blood through the leptomeningeal vessels. Areas of complete destruction may alternate with areas of atrophy and partial destruction.

Subdural hemorrhage produces adhesions between dura and pia, but they are threadlike, often passing from dura to pial vessel and rarely containing blood vessels. After such hemorrhage yellowing of the pia is still present many years after birth and widening of the intergyral fissures.

SUMMARY

Focal microgyria, meningocerebral cicatrix and the cerebral cicatrix of arterial occlusion are apt to produce seizures. On the contrary, we have not been able to prove that old subdural hematoma of itself is a cause of epileptic seizures. It may often be associated with other lesions and may be in a sense partly responsible for the associated intracerebral lesion which does produce epilepsy.

In considering the problem of initial cause in the case of any person with epilepsy, one must bear in mind the importance of minor cerebral lesions at birth and of thrombotic or inflammatory incidents in the febrile diseases of infancy, even though the onset of the seizures occurs only years afterward.

In the study of such cases simple anteroposterior roentgenograms of the skull should be examined for proportional decrease in the size of one side of the skull. This may be taken as suggestive evidence of an early lesion of the type we are considering (as in figure 7). Such lesions are often amenable to radical surgical therapy.

OBESITY IN CHILDHOOD

III. PHYSIOLOGIC AND PSYCHOLOGIC ASPECTS OF THE FOOD INTAKE OF OBESE CHILDREN

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Obesity may be defined as a nutritional state in which the storage of fat exceeds the amount that is commonly considered an expression of adequate alimentation. It is understood that the inordinate intake of food is only one factor among many which are important in the development of obesity. Some of the other factors have been or will be discussed in detail in other papers of this series. At present, I take their existence for granted but shall deliberately neglect them in this paper, wishing to focus attention on the dietary factor.

My observations will be presented in three sections, representing different aspects of the problem. In the first part the amount and composition of the food consumed, as described by the children and their parents, will be reported. Since the intake of food is a function of the body which does not occur entirely automatically but is influenced by free choice and habits, it is affected by numerous exogenous and endogenous factors. These will be dealt with in the second part which will be devoted to the regulation of the food intake and body weight. The management of obesity by manipulation of the diet will be discussed in the third part. Since the cooperation of the patient and his family is of great importance for the result of the treatment, my observations concerning this factor will be included in the third part.

In each section of the paper a short review of the relevant literature will precede my own observations.

I. FOOD INTAKE AS DESCRIBED

REVIEW OF THE LITERATURE

In reviewing numerous publications on obesity, I noted that more stress has been laid on faults in energy expenditure or on metabolic anomalies than on the errors of food intake. Many authors mentioned

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food only as a factor which, "of course," has to be considered but is of minor importance as compared with the underlying endogenous disturbance, which is frequently diagnosed as endocrine dysfunction. Some writers even stated that their patients were poor eaters who grew stout and remained so on exceedingly low diets. Such publications give the impression that their authors considered obesity a condition in which the law of conservation of energy does not hold true.

Concepts of this kind presuppose that the energy requirements and oxidation processes of an obese person are different from those of a normal person. Von Noorden's [1] differentiation between the obesity of exogenous and of endogenous origin is based on this conception. In "exogenous" obesity the food intake or energy expenditure or both are supposed to be markedly different from those of a normal person; whereas in "endogenous" obesity the actual economy of the metabolic processes is supposedly disturbed. The apparent simplicity of this classification made it popular for a whole generation, and it continues to be used by many in spite of increasing and well founded evidence against its correctness.

Food Intake of Adults.—The studies of Newburgh and Johnston [2] conclusively demonstrated that the energy exchange in obesity is normal. Undernutrition in an obese person results in a loss of weight exactly as predicted for a normal person. Water retention may temporarily mask the loss in weight during the first days or weeks of the experiment. Newburgh and Johnston's observations were made on various types of obese persons, and they concluded that all obesity is "simple obesity"; that is, excessive inflow of energy to the body is always the immediate cause of obesity.

Lauter [3] examined the various components of energy expenditure: basal metabolism, specific dynamic action of food and oxygen consumption during physical exercise. According to his observations, the caloric output of an obese patient is equal to or even surpasses that of a normal person in all respects. The positive metabolic balance, as expressed in the accumulation of fat, must result from an intake of food in excess of the requirements. In his experience, patients suffering from endocrine forms of obesity consume amazing quantities of food exactly as do patients with obesity due to causes other than endocrine dysfunction.

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1. von Noorden, C.: Die Fettsucht, ed. 2, Vienna, Alfred Hölder, 1910.

2. Newburgh, L. H., and Johnston, M. W.: Endogenous Obesity: A Misconception, Ann. Int. Med. **3**:815, 1930. Johnston, M. W., and Newburgh, L. H.: The Determination of Total Heat Eliminated by the Human Body, J. Clin. Investigation **8**:147, 1930.

3. Lauter, S.: Zur Genese der Fettsucht, Deutsches Arch. f. klin. Med. **150**: 315, 1926.

Most authors deal with the problem in a similar way. The output of energy is recorded in greater detail than direct observations of or inquiry into the feeding habits. Generally the conclusion that the food intake is excessive is drawn from indirect evidence: No abnormalities of energy metabolism can be demonstrated; the resorption from the alimentary tract in an obese person is not different from that of a normal person,[4] and undernutrition results regularly in a predictable loss of weight.[5] Murray, Dunlop and Lyon [6] inquired into the dietary habits of a large group of patients. They found that an excessively large and poorly balanced diet with a preponderance of starchy carbohydrates was, among all the factors under review, the one most commonly present. Lambie,[7] Campbell [8] and many others have reported similar observations.

Kisch [9] reported more thorough observations than the previously mentioned authors. He requested 50 obese patients to keep detailed records of their food consumption for twenty-four hours. According to forty-six of these records, the intake was extremely high, ranging from 2,900 to 3,500 calories. Thirty patients, while resting in bed, were fed a diet of 200 calories in excess of their basal requirements; 28 of these complained that this diet did not satisfy their appetite. Reviewing 258 clinical records, Kisch found that only 18 per cent contained a statement that the patient had been eating excessively; in 13 per cent the food intake was described as small. These statements had been made by the patients in good faith, and their exaggerated desire for food was never completely satisfied, although the food intake was larger than needed.

Food Intake of Children.—The references cited thus far deal with obesity in adults. Publications on obesity in children are less numerous and even less complete with regard to the record of dietary habits.

4. Neuenschwander-Lemmer, N.: Ueber Ausnutzungsversuche bei fettsüchtigen und normalen Menschen, Ztschr. f. d. ges. exper. Med. **99**:394, 1936.

5. (*a*) Evans, F. A., and Strang, J. M.: A Departure from the Usual Methods in Treating Obesity, Am. J. M. Sc. **177**:339, 1929. (*b*) Kenyon, J. H.: The Hypopituitary Type of Obesity Treated Without Glandular Medication, J. A. M. A. **101**:97 (July 8) 1933. (*c*) Short, J. J.: Extreme Obesity Followed by Therapeutic Reduction of Two Hundred and Thirty-Nine Pounds, ibid. **111**: 2196 (Dec. 10) 1938.

6. Murray, R. M.; Dunlop, D. M., and Lyon, M.: A Study of Five Hundred and Twenty-Three Cases of Obesity, Edinburgh M. J. **38**:561, 1931.

7. Lambie, C. G.: Obesity: Etiology and Metabolism, Brit. M. J. **2**:885, 1935.

8. Campbell, W. R.: Obesity and Its Treatment, Canad. M. A. J. **34**:41, 1936.

9. Kisch, F.: Ueber die Essucht Schweradipöser, Ztschr. f. klin. Med. **132**: 504, 1937.

Gordon [10] stated that in his experience overeating per se is an infrequent cause of obesity in children. Hess and Kunstadter [11] expressed themselves in a similar way, saying that obesity due to hyperalimentation is the exception rather than the rule. In both papers, however, dietary restriction was mentioned in the first place as necessary for effective treatment. Among 60 cases reported, Hering [12] classified only 1 as a case of obesity due to overfeeding.

Ellis and Tallerman [13] placed more emphasis on overeating. Obesity in the majority of their 50 cases was described as primarily exogenous in type, the patients showing a tendency to overeat, particularly with regard to carbohydrates. Hamburger [14] and his associates stressed the importance of overfeeding. Only 2 cases were reported in detail.[15] In their experience, overeating developed frequently as a habit during convalescence from some acute illness. Hamburger counted obesity among the habit disorders, which he described by the word *Ethismen* [16]; by this term he denoted a neurotic habit formation.

PERSONAL OBSERVATIONS

Description of Subjects.—My own observations [17] are based on information obtained from 142 obese children, 2 to 13 years of age, and from their parents. A detailed description of part of the group has been given in a previous publication.[18] At that time only 102 children were studied. Forty new patients have been added. The composition of the group has remained essentially the same with regard to age and racial distribution. When this study was made it comprised 75 girls and 67 boys. It must be emphasized that practically all children who came to my attention with obesity as a conspicuous clinical symptom

10. Gordon, M. B.: Endocrine Obesity in Children: Clinical and Laboratory Studies and Results of Treatment, J. Pediat. **10**:204, 1937.

11. Hess, J. H., and Kunstadter, R. H.: Diagnosis and Treatment of Obesity in Children, M. Clin. North America **22**:161, 1938.

12. Hering, S.: Die Formen der kindlichen Fettsucht und ihre Prognose, Monatschr. f. Kinderh. **73**:11, 1938.

13. Ellis, R. W. B., and Tallerman, K. H.: Obesity in Childhood, Lancet **2**:615, 1934.

14. Hamburger, F.: Polyphagia esthismatica, Wien. med. Wchnschr. **86**:772, 1936.

15. Frey, L.: Ueber zwei Fälle von Mastfettsucht im Kindesalter, Arch. f. Kinderh. **109**:1, 1936.

16. Hamburger, F.: Psychische Ethismen, Monatschr. f. Kinderh. **62**:191, 1935.

17. Miss Irene Waters, of the department of nutrition of Presbyterian Hospital, gave valuable assistance in collecting and evaluating the material.

18. Bruch, H.: Studies in Obesity in Childhood: I. Physical Growth and Development of Obese Children, Am. J. Dis. Child. **58**:457 (Sept.) 1939.

were included in this group, even though obesity was not always their chief complaint. I have excluded an 11 year old boy with Cushing's syndrome and have also refrained from attempting to use the data obtained from children who were mentally defective. Otherwise the group is comprehensive and includes several patients with obesity who might, I believe, be classified by other observers as having obesity of the hypopituitary, hypothyroid or cerebrally determined type.

The degree of obesity was recorded in percentage of weight excess as compared with the Baldwin-Wood tables.[19] These height-age-weight charts do not take into account the pubertal maturation. The importance of different pubertal ages for the height and weight at a given age has been demonstrated by Richey.[20] Since obese children, as a rule, mature earlier than nonobese children,[18] the calculated weight excess from ordinary height-weight tables gives only a rough estimate of the degree of the weight excess. The children were grouped according to the severity of the obesity. Children who were 20 to 39 per cent overweight were considered moderately obese. Thirty-two girls (42.5 per cent of the total number of girls) and 34 boys (50.5 per cent of the total number of boys) belonged to this group. Those who were 40 to 69 per cent overweight were considered severely obese. Thirty-four girls (45.5 per cent) and 27 boys (40.5 per cent) comprised this group. The remaining 9 girls (12 per cent) and 6 boys (9 per cent), who were 70 to 110 per cent overweight, were considered extremely obese.

Collection and Evaluation of Information.—An attempt was made to study the usual food intake of these children. In most instances the information was given by the parents, generally by the mother. Frequently the patients reported supplementary details or expressed a definite attitude toward a suggested change in the dietary habits. In a number of cases, visits by a social service worker were made to the home. The remarks of other members of the household and friends of the family served as a control for the correctness of the statements.

The tendency of obese patients to minimize the amount of their food intake was encountered frequently, both in the children themselves and in their parents. Detailed questioning about the consumption at different meals and especially about eating between meals generally revealed an approximately representative picture of the situation. One mother, whose first answer was "Just normal; he doesn't eat much," described

19. Baldwin, B. T., and Wood, T. D.: Weight-Height-Age Tables, New York, American Child Health Association, 1920.

20. Richey, H. G.: The Relation of Accelerated, Normal and Retarded Puberty to the Height and Weight of School Children, Monograph of the Society for Research in Child Development, National Research Council, 1937, vol. 2, no. 1.

the food situation at the end of the same interview as "I know; I stuffed him like a goose." She gave a vivid description of the large amounts which she was feeding her boy; since he did not always quite finish what she expected him to eat, it was "not much" in her opinion. In the analysis of the material children whose eating habits were described in this manner were counted among those with a high food intake. The description "normal" was accepted when detailed questioning at the first interview did not reveal any obvious deviation from what is generally considered adequate but not excessive for children of like age. In a number of cases further contact with the family showed that this description did not fit the actual situation. This discrepancy will be discussed later.

It was planned to obtain further information which might be used as a basis for an estimation of the amount of calories consumed. The older children, 8 years of age and more, were asked at the time of their first visit, before any dietary instruction had been given, to keep an exact and honest record of everything they ate and drank during the next week. Though a large number (more than 40) complied with the request, this record could be used for estimation of the caloric value of the food consumed in only a few instances. The description of the portions taken was too variable to permit a correct assessment of the real amount. The quantity described as "a tiny bit of mashed potatoes" by a 13 year old girl who was an enormous eater may in reality not have differed much from what another girl, whose total intake was much smaller, called a "very large portion of mashed potatoes baked." In a few instances when the menu consisted of items which were more standardized (like slices of bread, quarts of milk, etc.), estimation was possible. These food diaries, however, did yield information regarding the food preferences of these children. In addition, they proved helpful in arousing the interest of the patients in their eating habits.

Relation of Food Intake to Weight Increase.—A consideration of the weight curve of obese patients is important for a correct appraisal of the role of the food intake. The evaluation of this factor is complicated in children, since one is dealing with growing persons in whom a certain gain in size is normal. In this study a gain of weight was arbitrarily judged to be abnormal when it was more than 10 pounds (4.5 Kg.) a year in younger children. A statistical analysis of the reported increases in weight was not attempted, since the figures which were given by the parents were not always correctly remembered, nor was the time when the last weight had been taken. In some instances the weight at the time when the child entered school was remembered, which was sometimes several years before I saw him. In other cases the weight had been recorded at a previous visit to the general pediatric

clinic. The available figures, therefore, do not always refer to the time immediately preceding the examination. In all cases, however, the parents stated that the children were gaining constantly.

The recorded figures sometimes reflect a striking increase in body weight. One girl of 2½ years, who weighed 49 pounds (22.2 Kg.) when first seen, had gained 23 pounds (10.4 Kg.) during the preceding year. Another girl of 11 years, whose weight had been recorded by the school nurse, had gained 60 pounds (27.2 Kg.) in two and one-half years. An 11 year old boy who had been examined in the clinic before and who was markedly overweight gained another 25 pounds (11.3 Kg.) during the eight months before he appeared for treatment.

Most obese adults, after reaching a certain weight which is characteristic for them, keep their weight as constant as normal persons. Since their basal energy requirements are somewhat higher than normal, their food intake will be high, though not conspicuously so. During the period, however, when the condition develops and the body accumulates progressive amounts of fat, the energy inflow must be definitely above normal. In childhood, this developmental phase of the condition is the rule.

To illustrate the problems which have to be considered for an appraisal of the relation between food intake and weight increase, a pertinent case will be cited.

A boy 2 years and 4 months old, when first examined weighed 55 pounds (24.9 Kg.) and was 38½ inches (97.8 cm.) tall. He was 22 pounds (10 Kg.), or 66.6 per cent, overweight. Figure 1 demonstrates the severity of his condition. The diet which the mother described appeared to be adequate but not excessive. Apparently there existed a contradiction between the severity of the condition and this modest diet, which the boy had received from 1 year of age.

A review of the available data relating to the development of the obesity clarified this disharmony. The weight at birth was 7 pounds, 1 ounce (3,203 Gm.). The child weighed 34½ pounds (15,649 Gm.) when 6 months old and 42 pounds (19,051 Gm.) at 1 year of age. At 18 months the weight was 44 pounds (19,958 Gm.), and it was 52 pounds (23,587 Gm.) at 21 months. These increases as compared with those for the average weight development are graphically demonstrated in figure 2. It becomes immediately obvious that the period of excessive gain was during the first year of life. After that time, the rate of gain in weight was normal.

The feeding history reflects this course of the child's weight development. The mother, who is a conscientious woman but who has little control over the patient, gave him large amounts of milk as often as he wanted it. She said that he had refused to nurse. Vegetables and cereals were added early, and the patient ate large amounts of them in addition to drinking unlimited quantities of milk. When he was 1 year old, the parents became aware of the fact that he was too fat. His weight at that time was twice that of an average child of the same age. From that time on, he was fed a diet not larger than normal. He became adjusted to this lowered intake fairly well. He insisted on having milk, soups and

orange juice from the bottle until he was 2½ years old, and this habit was broken with great difficulty.

The patient has been followed in the obesity clinic for two years. His diet, which was normal when he was first seen, was somewhat reduced. He lost 5 pounds (2.3 Kg.) during the first few months. The mother had not enough control over the patient to keep him on a restricted diet for a longer period, and she increased his diet somewhat. He lost some weight during the following summer, when he was outdoors all day and actively playing. His weight curve

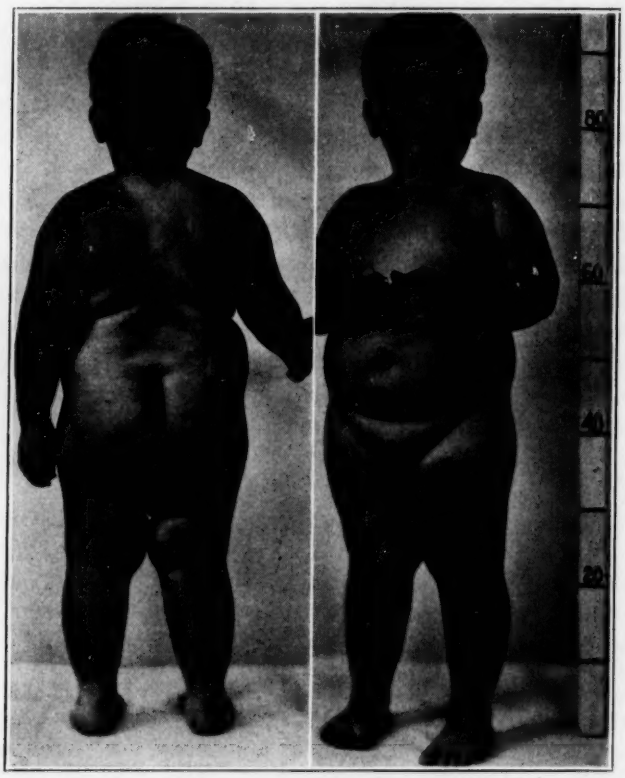

Fig. 1.—H. D., at the age of 2 years and 4 months. His height was 38½ inches (97.8 cm.), his weight 55 pounds (24.9 Kg.).

during these two years runs parallel with a weight curve which was constructed for his height (AV. WT.-HT. curve in figure 2). Throughout the period of observation, the boy was approximately 4 inches (10 cm.) taller than the average boy of his age. The rate of growth during this period was normal. One may assume that the excess growth had occurred during the period of rapid gain in weight.

Although the boy is still markedly overweight (22 pounds [10 Kg.], or 52 per cent), his present rate of growth and gain in weight are in good agreement with those of nonobese children on a normal diet.

Information About Food Intake. — Although the information obtained by questioning the patients and their parents may not completely describe the feeding habits, it was felt that in most instances the information correctly expressed the situation or else reflected the attitude of the parents or patients toward food. No detailed information was obtained for 2 girls and 4 boys. The following statements about the quantity and the quality of the food intake of 73 girls and 63 boys are based on the histories (table 1).

Large Food Intake: The quantity of food consumed was described as large for 57 girls and 43 boys, that is, for 74 per cent of all children.

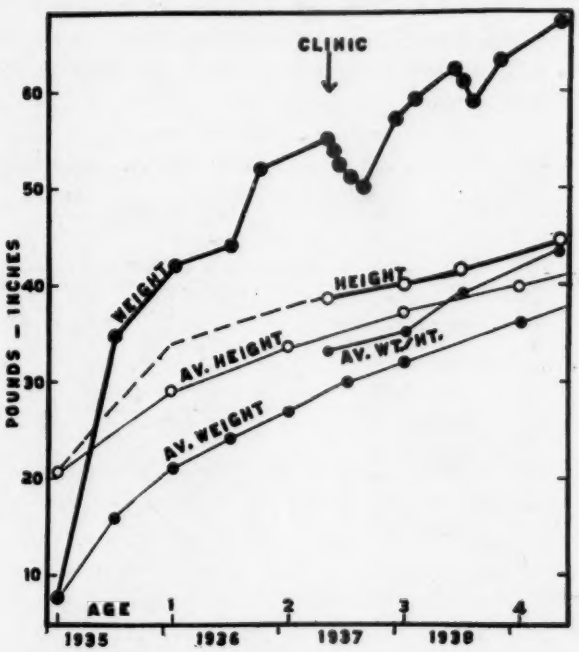

Fig. 2.—Chart showing the height and weight development of H. D., born February 1935. The line *Av. wt./ht.* represents the average weight for his height. The interrupted part of the height line indicates the assumed height development during the first year of life.

The quantitative term "large" has been used to denote the food intake when the amount described was definitely above that recommended in the clinic for the nutrition of normal children. In the majority of cases the response that the intake was large was evoked immediately when a question about the appetite and food intake was asked. The terms used for depicting the amounts eaten varied a good deal; they ranged from "good appetite" and "he eats very well" to "most tremendous appetite,"

"he eats voraciously" and "food is the only interest she has." Sometimes the statements obviously reflected the attitude of the mother toward this fact. There are the proud statements, like "She drinks 2 quarts of milk for me and has the most wonderful appetite" (a 3 year old girl who weighed 70 pounds [31.8 Kg.]) and "The neighbors call her in if their children won't eat; she can eat all the time, and plenty of it" (another girl of 3 years who weighed 60 pounds [27.2 Kg.]). Other mothers were less content with the large amounts which their children consumed and complained about their uncontrollable appetites. One stated: "He is always hungry; he wants to eat constantly—he never gets enough" (a 10 year old boy who was 90 per cent overweight and gaining rapidly). All children whose food intake was described as large had been gaining weight excessively before they were examined.

TABLE 1.—*Quantity of Food Intake of One Hundred and Thirty-Six Obese Children*

Food Intake as Reported	Girls		Boys		Boys and Girls	
	Number	Per Cent	Number	Per Cent	Number	Per Cent
Large	57	78.0	43	68.5	100	74
Reduced intentionally	4	5.5	4	6.0	8	6
Normal	10	13.8	10	16.0	20	14
"Poor appetite"	2	2.7	6	9.5	8	6

In all instances more detailed information about the actual food intake was obtained; in no case did the descriptive term represent an overstatement. As far as an assessment of the caloric value was possible, it ranged between 2,500 and 4,000 calories, even on low estimates. I do not offer detailed figures obtained in individual cases, since the assessments could not be made with great accuracy. The report of a large number of figures would give the pretense of an accuracy which this material does not possess.

The food intake of 26 per cent of the children, 16 girls and 20 boys, did not deviate appreciably from that of normal children or was even described as small. This group calls for a more detailed discussion.

Deliberate Reduction of Food Intake: For 8 children, 4 boys and 4 girls, the reported normal food intake was explained by attempts at reducing which had been carried out with more or less success. One boy of 11 years had lost weight during the past year; the rate of gain of the other children had slowed down since the diet had been altered. That a child continued to be stout in spite of a small food intake was generally a source of concern for the parents or the school.

If the children whose food intake was reduced in an attempt to lose weight are added to those whose food intake has been desecribed as large, the total number of children whose family recognized the unusual desire for food is 108, or 80 per cent of children for whom information regarding the quantity of the food consumed was recorded.

Normal Food Intake: For 20 children, 10 boys and 10 girls, the information was given that they did not eat more than other children. Three boys showed a weight development similar to that of the boy in the case already reported in detail. There had been a period of rapid gain in the past but only a normal gain in recent years. All 3 boys were only moderately overweight. Although the parents had not deliberately changed the diet, apparently a similar adjustment had taken place.

The other 17 children had been gaining progressively prior to their attendance at the clinic. The information about these children was characterized by evasiveness and a defensive attitude on the part of the parents and patients. From none of these patients were the detailed food diaries obtained, so that the statement "normal" expresses only the opinion of the mother. At the same time there was pronounced resistance against any dietary advice. One mother, when told to give her daughter less candy and cake and more wholesome food, declared, "It is depriving the child too much not to let her have it." A father who repeatedly asserted that his daughter gained rapidly on practically no food was disgusted when a change in the diet was suggested. "I brought her to the clinic to lose weight, not for a diet," he said. The older sister accompanied this patient at another visit and told how the younger girl ate more at mealtimes than she and a brother ate together; she added that the patient ate constantly between meals and that the parents had no control over her.

Only a few children of this group were followed for any length of time. In most cases the subsequent appointments were broken as soon as a change in the dietary habits was discussed. A social worker who went to the home of some of these children was told in all instances that "since food had not made the children fat," the parents did not want to have anything changed about the diet. In other cases, in which the patients apparently cooperated well, the loss of weight was not adequate and not in agreement with the calculated caloric intake. One boy of 11 gained 30 pounds (13.6 Kg.) in eight months while he was supposedly eating a diet of 1,000 calories. He was admitted to the hospital. During three and one-half weeks he lost 15 pounds (6.8 Kg.) while eating the general hospital diet in amounts larger than what had been repeatedly described as his usual intake. Only then did he admit to numerous digressions from his prescribed diet. Another patient came to the hospital for a tonsillectomy. The mother came to call for him during lunch time and was upset when she saw the portions which

were served to all children. She complained that it was impossible for her boy to exist on so little food and that he was used to eating at least twice as much. Previously she had stated repeatedly that she gave him little to eat and that his diet was smaller than average.

In all cases in which there was an opportunity to check the information given by the parents, the food intake was found to be much larger than had been stated. In other cases in which the children could not be followed, the resistance against any proposed change was so great that one had good reason to assume that the food intake was "normal" only in the opinion of the parents.

Small Food Intake: Finally, 8 patients, 6 boys and 2 girls, whose parents complained about the "poor appetite" of their children, must be mentioned. The 2 girls were only moderately overweight, and their rate of gain was not excessive. In both cases there was marked overconcern relating to all bodily functions, not only to food intake, and both children had been forced to eat from infancy.

Of the 6 boys, 1 was extremely obese (more than 70 per cent overweight), 3 were severely obese, and 2 were moderately so. All of them had been gaining weight progressively during the last year. The attitude of the parents of these boys was similar to that of the parents who described the food intake as normal. There was a marked conflict between the concern over the physical condition on the one hand and the fear that a low food intake might be harmful on the other. Three of the mothers were extremely dull; they constantly reiterated, "He don't eat nothing," without being able or sufficiently interested to give detailed information. Their resistance against advice with regard to feeding habits and better arrangement of the meals made any attempt at management hopeless. One mother, who had been told previously that her boy suffered from an endocrine disorder, refused to give any information beyond "he eats too little anyway—and he needs injections." The boy drifted to another clinic and received injections of a gonadotropic substance from the urine of pregnant women (antuitrin S) for the next year; he gained 19 pounds (8.6 Kg.) during that period. The mother refused to restrict his food intake which, even unrestricted, did not satisfy her idea of the amount her boy should eat. In the remaining 2 cases continued contact with the family revealed that the patients had been eating large amounts of food previously and that the term "poor appetite" applied only to a recent, temporary change in the eating habits.

In all these cases the information of a low food intake is the expression not so much of the true feeding habits but of the exaggerated expectation of the parents, all of whom showed marked overconcern in other respects also.

Reviewing the information on the quantity of food consumed by obese children, one may conclude that the food intake is decidedly

greater than normal during periods of excessive weight increase. It is not necessarily different from that of normal children at times when the weight is stationary or is increasing at a normal rate, although the patient continues to be overweight.

Composition of Diet.—For an understanding of the eating habits of obese children, it is necessary to know not only how much but what they eat. The composition of the diet showed in a great number of cases an astonishing uniformity. Nearly all children overate on starchy food. Bread, cake, ice cream, candy and soups ranged first in all diet lists. For example, 1 boy of 10 recorded six slices of bread, as sandwiches, a piece of cake, four apples and five bananas as a regular lunch, in addition to several glasses of milk, of which he would take 2 quarts a day. For Italian children spaghetti and macaroni played an important role. Many Jewish children added sour cream to each meal. A few younger children drank large quantities of milk, 2 quarts a day or more. One mother had been concerned about the large quantities of water which her child drank. "I thought the water blew her up, so I gave her milk instead," she explained. On the whole, milk did not count among the favorite foods. In a great number of cases the dislike for milk was given as one reason for the addition of cake and other sweets to the diet. In her eagerness to make her child drink the "required" quart of milk per day, the mother would bribe him with all kinds of tidbits, and soon a firm habit was established; the milk was taken only as an addendum to the cake or only after chocolate syrup or some other "nourishing" substance had been added.

The question about the kind of food which the child ate was usually answered by "everything," but detailed questioning proved in each case that this statement was incorrect. Not one child in the whole group had learned to eat a mixed, well balanced diet. Vegetables and salads led in the series of foods which were disliked. Fruits, with the exception of bananas and orange juice, came next. The attitude toward meat varied: Some children liked large amounts; others were extremely fussy. The mother of a 12 year old girl who was 45 per cent overweight asked, "But is she allowed to have other but white meat? Isn't dark meat too heavy for her?" Many of the younger children, up to 6 and 8 years old did not want to chew, especially when they had been bottle fed long beyond infancy. An 11 year old boy received only mashed meat and vegetables, mostly carrots and peas, to make them look "littler" so that he would eat them. None of the children was allergic to eggs, but few had received them regularly in their diet. Most children soon complained about the monotony of an egg for breakfast every day, and refused to take it.

Feeding Habits.—It was felt in the beginning that the main reason for the preponderance of starchy food was economic, since carbohydrates are the cheapest provider of energy. In a number of cases this opinion found support in the fact that the onset of the obesity had coincided with a change in the economic status of the family. The resistance shown against any change in the diet, however, was not on an economic basis. In cases in which the financial status was poor the family was advised not only about a well balanced diet but about economical ways of shopping, so that the new diet could be provided at even lower cost than the previous one with its large amount of cake and sweets. In such cases it appeared obvious that the one-sided composition of the diet had developed not from financial considerations alone but rather from the inability or unwillingness of the patient (or his parents) to give up previously acquired habits and to add new experiences. The pronounced likes and dislikes for certain foods which are observed so regularly in these children may be described as representing an early, infantile phase of taste development; economic considerations were only a contributing factor.

The same lack of training and adjustment to social requirements is reflected in the tendency to eat between meals. Not one of these children ate at mealtimes only; in a few instances there was no adherence to regular mealtimes. These children were used to receiving or taking food whenever they wanted it. In many cases the caloric value of the food eaten between meals exceeded that of food taken at mealtimes.

COMMENT

From the numerous reports which show that the caloric requirements of obese persons are not fundamentally different from those of normal persons, an observation which I also found to be true in my group of patients,[21] one might predict that the food intake would be congruent with the weight curve, that it would be conspicuously high in periods of rapid gain in weight and normal or only slightly above normal in periods of constancy of weight or normal rate of gain. In view of the great uncertainty as to whether this expectation holds true in actual clinical observation, and in view of the frequent statements to the contrary, it appeared advisable to evaluate the eating habits of a large group of obese children. My observations bear out the correctness of the conclusion that food intake and increase in weight are correlated.

This statement of fact does not, however, clarify the underlying cause of the condition. The discovery of a high food intake merely represents another aspect of the same clinical problem; it is only one of the mechani-

21. Bruch, H.: Obesity of Childhood: II. Basal Metabolism and Serum Cholesterol of Obese Children, Am. J. Dis. Child. **58**:1001 (Nov.) 1939.

cal factors by which the body accumulates the large deposits of adipose tissue. For an understanding of the increased desire for food or the tendency of the body to grow beyond normal dimensions, a discussion of the mechanism by which the body regulates its food intake and weight is necessary.

II. REGULATION

Physiologic Aspects

REVIEW OF THE LITERATURE

Hunger and Appetite.—The bodily sensations which lead to the intake of food are hunger and appetite. Though often confused, they are essentially different—in physiologic basis, in localization and in psychic elements. Cannon [22] and Carlson [23] studied extensively the physiologic basis of the sensation of hunger. I shall follow these authors in describing the differences between the two sensations.

Hunger is felt as a dull ache or gnawing pain referred to the lower sternal region and the epigastrium. It is caused by periodic contractions of the empty stomach, which do not begin until after the stomach has been empty for some time. Appetite is related to previous sensations of taste and smell of food; it has important psychic elements in its composition. Hunger is a primitive elemental sensation which imperiously demands relief; appetite implies wishing, longing or yearning for something especially desirable. The person influenced by an appetite is tempted; he seeks satisfaction and wishes to renew previous pleasures. Hunger may be abolished by the first few mouthfuls of a meal, while the appetite still calls. Thirst is similar to hunger as a powerful, persistent stimulus which demands relief. The appetite for drink closely resembles the appetite for food, with all its psychic implication.

Hunger contractions of the stomach occur when the sugar content of the circulating blood falls about 25 per cent. Appetite is stimulated by the memory, smell or sight of agreeable food. At present no evidence is available indicating that any specific bodily change underlies the sensation of appetite. The initial secretion of gastric juice ("psychic secretion") is stimulated by appetite (Pavloff [24]). Although the two sensations thus may exist separately, they nevertheless have the same function of leading to the intake of food, and they usually appear together. The cooperation of hunger and appetite is probably the reason for their being so frequently confused. In clinical work it is not always possible to differentiate between the two sensations.

22. Cannon, W. B.: Bodily Changes in Pain, Hunger, Fear and Rage, ed. 2, New York, D. Appleton and Company, 1929.

23. Carlson, A. J.: The Control of Hunger in Health and Disease, Chicago, University of Chicago Press, 1916.

24. Pavloff, I. P.: The Work of the Digestive Glands, translated by W. H. Thompson, ed. 2, London, C. Griffin & Co., 1910.

Cooperating with hunger and thirst is the sensation of having had enough. It protects the organism against being overstocked with food and water. The feeling of satiety is little understood; it involves the element of contrast between the uncomfortable tension of hunger and the sensation of fulness, together with the lingering memories of the taste and smell of food. The sensation of satiety does not function adequately in obese subjects.

Growth and Food Intake.—It is a truism to say that the intake of food is determined by the needs of the individual. These needs may have a physiologic or a psychologic origin. Under pathologic conditions, such as diabetes mellitus or exophthalmic goiter, the metabolic disturbance results in an increased urge for food. The rapidly growing young organism requires more energy per unit of body weight than the fully grown. If the rate of growth and development exceeds the average, the need for food rises correspondingly. Kerr [25] described a case of pubertas praecox in a 6 year old girl in whom a voracious appetite had been conspicuous from infancy. The dog in which Putnam, Benedict and Teel [26] produced acromegaly by injection of anterior lobe pituitary extract differed from its litter mate, among other ways, in its consumption of enormous amounts of food. At autopsy this dog showed an almost complete absence of subcutaneous and omental fat. These observations show that abundant ingestion of food results in accumulation of fat deposits only when the intake is in excess of the metabolic and structural needs of the body.

The rate of growth of obese children exceeds that of normal children; [18] I am not able to state on the basis of my observations whether this increased rate of growth is the cause or the result of the copious intake. It is probable that one is dealing with allied factors which are determined by the same or by closely related central stimuli. The food intake, however, is far in excess of the demands of the organism for growth, and the surplus is stored as fat deposits.

Cortical Innervation and Morbid Hunger.—Disturbances in the cortical innervation may cause morbid hunger, or bulimia. The older literature recorded several cases of hunger of this type. Mill [27] reported in 1887 the case of a 16 year old boy with a tumor of the second frontal gyrus and wrote: "He was ravenously hungry during his illness and bolted his food at all times." Spiller [28] reported similar observations in

25. Kerr, W. L.: A Case of Pubertas Praecox, Brit. M. J. **2**:620, 1937.

26. Putnam, T. J.; Benedict, E. B., and Teel, H. M.: Studies in Acromegaly: VIII. Experimental Canine Acromegaly Produced by Injection of Anterior Lobe Pituitary Extract, Arch. Surg. **18**:1708 (April) 1929.

27. Mill, C. K.: Two Cases of Brain Tumor, J. Nerv. & Ment. Dis. **14**: 707, 1887.

28. Spiller, W. G.: Brain Tumor, J. A. M. A. **53**:2078 (Dec. 18) 1909.

1909. More recently, Frazier [29] mentioned this symptom in a series of cases of tumor involving the frontal lobe.

In other cases that have been reported, morbid hunger developed after injury to the head. Paget [30] reported 14 cases—13 culled from the literature and 1 case observed by himself—"of voracious hunger and thirst from injury or disorder of the brain." Sollier and Delagenière [31] observed morbid hunger in an 11 year old boy who had suffered cranial trauma. In this case the condition persisted for more than three months; nothing could alleviate the boy's inordinate desire for food. No mention is made as to whether the body weight changed during that period. Fulton and his co-workers [32] recorded increase of the hunger sensation in monkeys in which experimental lesions of the brain had been produced. Lesions of the prefrontal area were associated with ravenous hunger, which sometimes involved ingestion of two or three times the normal amount of food. Despite this circumstance the animals lost weight. They exhibited another striking condition characterized by a great increase in spontaneous motor activity. Fulton assumed that the sensation of morbid hunger may be due to increased motility of the stomach. Watts [33] observed that stimulation of the premotor area caused vigorous peristalsis of the whole gastrointestinal tract, so that the food was hurried through the alimentary canal.

It is probable that the ravenous hunger of some idiots and other persons mentally defective is due to irritation or destruction of the intestinal representation in the cortex or of tracts originating there. Obese children with obvious mental defect were excluded from my studies.

The problem of increased desire for food in mentally normal obese children is different, however, from the mechanism just described. Although many children have ravenous appetites which are uncontrollable under the conditions of their homes, decreased ingestion of

29. Frazier, C. H.: Tumor Involving the Frontal Lobe Alone: A Symptomatic Survey of One Hundred and Five Verified Cases, Arch. Neurol. & Psychiat. **35**:525 (March) 1936.

30. Paget, S.: On Cases of Voracious Hunger and Thirst from Injury or Disease of the Brain, Tr. Clin. Soc., London **30**:113, 1897.

31. Sollier, P., and Delagenière, H.: Le centre cortical des fonctions de l'estomac d'après un cas d'abcès du cerveau d'origine traumatique, Rev. neurol. **9**:1103, 1901.

32. Fulton, J. F.; Jacobsen, C. F., and Kennard, M. A.: A Note Concerning the Relation of the Frontal Lobes to Posture and Forced Grasping in Monkeys, Brain **55**:524, 1932. Fulton, J. F.: Some Functions of the Cerebral Cortex: Anatomic Representation in the Cerebral Cortex (Beaumont Lecture), J. Michigan M. Soc. **33**:175, 1934.

33. Watts, J. W.: The Influence of the Cerebral Cortex on Gastro-Intestinal Movements, J. A. M. A. **104**:355 (Feb. 2) 1935.

food is not associated with symptoms comparable to the irresistible urgency of morbid hunger. The discomfort of the obese patient on a reducing regimen is rarely due to a true hunger sensation; it is the dissatisfaction of a person accustomed to having his desires and wishes fulfilled who suddenly meets denial. Within a few days, most obese patients adjust to the lower intake.[5] Apparently the disturbance in appetite in the obese can be influenced from without, and the organism can satisfy its metabolic needs by drawing on its stores of fat.

Hypothalamic Regulation of Food Intake.—The regulation of food intake by the central nervous system is not limited to the cerebral cortex. Another central representation has been discovered in the vegetative nuclei of the hypothalamus, the tuber cinereum and the walls of the third ventricle. Experimental lesions in the region of these vegetative centers can be associated with adiposity. Most authors who succeeded in producing experimental obesity in animals through well defined local lesions (Bailey and Bremer,[34] Smith [35] and others) did not mention changes in the appetite of the animals, however. Keller and Noble [36] and Ransom, Fisher and Ingram [37] noted the great greediness and polyphagia of the animals in which adiposity developed after hypothalamic or infundibular lesions. In one dog, Keller and Noble observed enhanced appetite both for milk and for solid food which continued until a new level for body weight was reached by the deposition of fat, after which the food intake returned to normal. This observation is in good agreement with the clinical course of obesity, which in many cases has been found to be a self-limited disorder.

The comparative neglect with which appetite and food intake have been treated as factors in the development of adiposity is in distinct contrast to the attention which thirst and fluid intake have received as symptoms of diabetes insipidus. Obesity and diabetes insipidus have many parallel features, and they may occur together as manifestations of lesions at the base of the brain. An outstanding difference in the mechanism of these two disorders arises from the circumstance that in diabetes insipidus fluid is excreted in excessively large amounts through

34. Bailey, P., and Bremer, F.: Experimental Diabetes Insipidus, Arch. Int. Med. **28**:773 (Dec.) 1921.

35. Smith, P. E.: The Disabilities Caused by Hypophysectomy and Their Repair: The Tuberal (Hypothalamic) Syndrome in the Rat, J. A. M. A. **88**: 158 (Jan. 15) 1927.

36. Keller, A. D., and Noble, W.: Adiposity with Normal Sex Function Following Extirpation of the Posterior Lobe of the Hypophysis in the Dog, Am. J. Physiol. **113**:79, 1935; Further Observations on Enhanced Appetite with Resultant Adiposity Following Removal of the Posterior Lobe of the Hypophysis, ibid. **116**:90, 1936.

37. Ransom, S. W.; Fisher, C., and Ingram, W. R.: Adiposity and Diabetes Mellitus in a Monkey with Hypothalamic Lesions, Endocrinology **23**:175, 1938.

the kidneys and is therefore lost to the body; hence the urge for more fluid is a conspicuous symptom. In obesity the superfluous intake is retained in the fat deposits and can be utilized again for the energy metabolism if need arises. The symptoms of hunger and appetite in obese persons are therefore less pronounced, and the whole process is reversible. Fat storage, however, is not an entirely passive process determined only by the supply.

Neural Regulation of Fat Storage.—Recent experimental studies on neural regulation of fat deposits in connective tissue carry convincing evidence that fat storage and mobilization are regulated through neural influences. Hausberger [38] resected the nerves of the fat bodies of mice and rabbits on one side, leaving the other side intact. The fat bodies are special fat masses, with separate nerve supply, which occur at the side of the neck or between the scapulas of some mammals. Within three to five weeks, an enormous amount of fat accumulated on the denervated side. The nerveless fat body continued to store fat even during periods of starvation, until nearly all other deposits were exhausted; the last available reserves, however, were depleted sooner from the denervated side. In subsequent studies he showed that the increased storage of fat took place only during the first period after sympathectomy and that in a later phase both storage and mobilization were decreased. Beznák and Hasch [39] made similar observations. Unilateral splanchnicotomy in cats and rats resulted in the deposition of fat in the perirenal tissue to such an extent that it weighed 100 to 300 per cent more than the perirenal fat tissue on the intact side. The authors drew the conclusion that, in consequence of the splanchnicotomy, changes took place in the perirenal connective tissue which slowed both the deposition of fat and its mobilization; the mobilization was retarded more than the deposition.

Since the hypothalamus initiates nerve impulses which are discharged through the autonomic nerves,[40] one may surmise from these observations that the deposition of fat is regulated from the midbrain. Adiposity following lesions in the region of the hypothalamus may be considered as a sequel to the altered tonus in the innervation of the adipose tissue. Further study in this direction may eventually lead to an understanding of the various localizations of the fat deposits.

It is not inconceivable that the increased desire of some obese patients for food is secondary to the change in the fat metabolism.

38. Hausberger, F. X.: Ueber die nervöse Regulation des Fettstoffwechsels, Klin. Wchnschr. **14**:77, 1935; Ueber Veränderungen des Fettumsatzes im entnervten Fettgewebe, Arch. f. exper. Path. u. Pharmakol. **192**:70, 1939.

39. Beznák, A. B. L., and Hasch, Z.: The Effect of Sympathectomy on the Fatty Deposit in Connective Tissue, Quart. J. Exper. Physiol. **27**:1, 1937.

40. Ransom, S. W.: Some Functions of the Hypothalamus, in Harvey Lectures, 1936-1937, Baltimore, Williams & Wilkins Company, 1937, p. 92.

Specifically, this mechanism may play a role in all those clinical conditions in which adiposity develops suddenly in the course of a disease involving the hypothalamic region. Fulton and Bailey [41] considered adiposity a part of the hypothalamic syndrome caused by tumors in the region of the third ventricle, a syndrome which includes also hypersomnia, polyuria, genital dystrophy and perhaps also glycosuria and circulatory disturbances. It is more than likely that the case described by Fröhlich [42] belongs to the same class; Fröhlich's assumption that the syndrome was due to a lesion of the pituitary gland has not been borne out by subsequent observations.[43]

I do not wish to review here the extensive literature on the relation between the endocrine glands and adiposity. Wilder [44] summarized the subject in 1932 and concluded: "When all is said on the score of the endocrine glands, it leaves one with the impression that the role in the production of obesity has been astonishingly overestimated." In spite of the progress made in the study of the endocrine glands in recent years, this statement still holds true. I should like to add from unpublished observations on a large group of children with hypothyroidism that interruption of thyroid medication is regularly followed by a loss of appetite.

Pathologic lesions in the hypothalamic region which may be associated with adiposity are neoplasms, as mentioned before, or sequels of encephalitis [45] or chorea.[46] The incidence, however, of such demonstrable organic causes among the large number of patients suffering from obesity is certainly small. No fundamental difference in the energy exchange has been discovered in the course of the condition, whether or not an organic lesion has been found. Freyberg and Newburgh [47] found in a case of verified pituitary basophilism that undernutrition caused a loss of weight exactly as predicted for a normal person. Kisch [9] observed a 15 year old boy with a tumor in the region of the hypophysis

41. Fulton, J. F., and Bailey, P.: Tumors in the Region of the Third Ventricle: Their Diagnosis and Relation to Pathological Sleep, J. Nerv. & Ment. Dis. **69**: 1, 145 and 261, 1929.

42. Fröhlich, A.: Ein Fall von Tumor der Hypophysis cerebri ohne Akromegalie, Wien. klin. Rundschau **15**:883 and 906, 1901.

43. Bruch, H.: The Fröhlich Syndrome: Report of the Original Case, Am. J. Dis. Child. **58**:1282 (Dec.) 1939.

44. Wilder, R. M.: Regulation of Weight of the Body, Internat. Clin. **1**: 30, 1932.

45. Duncan, A. G.: The Sequelae of Encephalitis Lethargica, Brain **47**: 76, 1924. Walsh, T. G.: Postencephalitic Obesity, J. A. M. A. **87**:305 (July 31) 1926.

46. Evans, P. R.: Obesity Following Chorea, Brit. J. Child. Dis. **34**:179, 1937.

47. Freyberg, R. H., and Newburgh, L. H.: The Obesity and Energy Exchange in a Verified Case of Pituitary Basophilism, Arch. Int. Med. **58**:229 (Aug.) 1936.

who presented the classic picture of dystrophia adiposogenitalis and in whom dietary restriction was followed by a marked loss in weight.

Pathogenesis of Obesity.—The similarity between obesity of known central origin and simple obesity makes it likely that analogous mechanisms are involved in the production of the condition. Wilder [44] expressed the opinion that simple obesity may be due to functional derangements of the same centers which are involved in organic lesions. The polyphagia may be produced either by abnormally intense stimulation of normal "appetite centers" or by stimuli of normal intensity acting on hyperirritable "appetite centers." Wilder further stressed the importance of hereditary factors. Bauer,[48] discussing "pseudoendocrine obesity," considered a specific constitution, usually inherited, as the basic disturbance. The main expression of this constitutional anomaly is the increased tendency of the tissues to store fat; this tendency is, however, influenced by neural and hormonal stimuli. Kisch [9] concluded that the pathologic appetite of obese patients is due to a "diencephalic weakness" in which the desire for food persists in spite of ingestion of adequate quantities, since the feeling of satiety is delayed or is not produced at all.

In spite of the differences in phraseology these concepts are in agreement with each other and with previously cited evidence from animal experiments. My own hypothesis concerning the pathogenesis of obesity follows a similar line of thought.

PERSONAL OBSERVATIONS

In my group of 142 children there was only 1 patient who had suffered from encephalitis. In no other case did careful history or clinical examination with the usual methods succeed in establishing the diagnosis of an organic lesion at the base of the brain. Many children, however, exhibited vegetative symptoms, such as slight disturbances in temperature regulation, in perspiration and in vasomotor control, all of which might be referred to some functional disorder in the autonomic centers. More impressive were changes in the behavior which sometimes closely resembled the behavior of children after encephalitis.

These similarities in behavior stimulated a search for a factor which might give meaning to the "functional disorder" and "constitutional weakness" of other authors. The emotional development may be of importance in calling into play the functional disturbance of the hypothalamus. The fundamental role of the hypothalamic functions in transforming psychologic experiences into somatic manifestations has been recognized during the last decade.[49] A theory which attributes to

48. Bauer, J.: Pathologie der Fettsucht, Med. Klin. **29**:1297, 1933; Pseudoendokrine Fettsucht, Wien. klin. Wchnschr. **49**:600, 1936.

49. Grinker, R. R.: Hypothalamic Functions in Psychosomatic Interrelations, Psychosom. Med. **1**:19, 1939.

emotional stimuli etiologic significance in the development of a somatic condition is well supported by experimental evidence. It has been one of the aims of this study to collect clinical observations to confirm this conception further.

Psychologic Aspects

Review of the Literature

Emotional Factors and Obesity.—That obesity may be associated with psychic changes has been recognized by many. Those reports which describe changes in the character as part of the symptomatology of obesity will not be discussed here. In a number of publications the presence of obesity is indiscriminately considered an expression of pituitary disorder; the psychic changes are accordingly regarded as an expression of pituitary dysfunction. For example, Weygandt,[50] whose paper is widely cited in the literature, described as characteristic of pituitary obesity mental changes observed in a group of patients who either were mentally defective, even to the extent of idiocy, or suffered from a progressive organic disease of the central nervous system. Papers of this type are numerous; they will not be enumerated here, since they do not help in the understanding of the problems.

There is a smaller group of publications in which emotional imbalance in its etiologic relation to the development of obesity is considered. During and after the World War, Lichtwitz[51] observed rapidly developing obesity in women who had been under severe mental stress. He rejected the explanation of the obesity and mental changes as a sequel to thyroid dysfunction and stressed the importance of the parallel influence of the emotional state on the metabolism and the psyche.

The case of a young woman who suffered from a number of symptoms characteristic of severe disturbance in the midbrain was reported by Lützenkirchen.[52] After long-standing, traumatic, psychic experiences, this patient gained weight rapidly during her second pregnancy; subsequently she suffered from tormenting thirst, and the clinical picture closely resembled diabetes insipidus. Amenorrhea persisted for several years after delivery, and on later examination the uterus was found to have become atrophic. Endocrine treatment in all available forms did not influence the condition. However, these symptoms disappeared after her emotional conflicts were solved. She remarried and became pregnant again. The thirst diminished rapidly, and she lost 58 pounds

50. Weygandt, W.: Psychische Störungen bei hypophysärer Fettsucht, München. med. Wchnschr. **68**:1356, 1921.

51. Lichtwitz, L.: Ueber die Beziehung der Fettsucht zur Psyche und Nervensystem, Klin. Wchnschr. **2**:1255, 1923.

52. Lützenkirchen, S.: Dystrophia adiposa-genitalis nach psychischem Affekt, München. med. Wchnschr. **71**:1577, 1924.

(26.3 Kg.) during this pregnancy. Mental excitement, however, continued to be associated with an increased sensation of thirst.

According to Newburgh [53] the traditional concept that obese people are jovial happy-go-lucky persons who simply enjoy their food is wrong. He cited several instances in which the patient obtained relief during periods of nervous stress by repeated nibbling of food. "Many of these people," he explained, "have a passion for food which is as deep as it is in the chronic alcoholic addict for alcohol. I want to emphasize that type of individual who uses food as a comfort, as a means of combating unpleasant circumstances." Harrington [54] brought further evidence that overeating in obese persons is closely allied with nervous tension. Lesses and Myerson [55] reported a series of 12 cases in which benzedrine sulfate proved helpful in the treatment of obesity. They observed that a certain type of obesity was due to a disturbance in the mood which upset the appetite-regulating mechanism. Increased eating in such cases was considered not to be true hunger but a compensation for the disturbed mood. Benzedrine sulfate was effective by improving the mental state, by depressing the appetite and increasing the physical activity. Hochman [56] reported 6 cases in which a connection between periods of overeating and times of emotional disturbance was apparent. In his opinion compulsive eating is part of a defense mechanism for combating anxiety.

Emotional Significance of Food.—In addition to these references, a few studies which deal with the emotional significance of food, without special relation to obesity, will be discussed. Appetite as described by the physiologists [57] is characterized by its psychic elements. It has been included in the studies of the physiologists in its relation to "conditioned reflexes." [24] Schilder [58] conducted experiments on conditioned reflexes in human beings which made it clear that one is dealing with complicated psychic processes and adjustments. Many factors in the feeding histories which on superficial observation appear to be simple reflex mechanisms and habit formations frequently represent important emotional manifestations of the person.

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53. Newburgh, L. H.: The Cause of Obesity, J. A. M. A. **92**:1659 (Dec. 5) 1931; personal communication to the author, 1939.

54. Harrington, M. M.: Appetite in Relation to Weight, J. Am. Dietet. A. **6**:101, 1930.

55. Lesses, M. F., and Myerson, A.: Human Autonomic Pharmacology: XVI. Benzedrine Sulfate as an Aid in the Treatment of Obesity, New England J. Med. **218**:119, 1938.

56. Hochman, S.: Mental and Psychological Factors in Obesity, M. Rec. **148**: 108, 1938.

57. Cannon.[22] Carlson.[23]

58. Schilder, P.: Conditioned Reflexes, Arch. Neurol. & Psychiat. **22**:425 (Sept.) 1929.

Hall [59] studied the development of various health habits in children of different nationalities. Jewish children showed greater difficulty in establishing satisfactory feeding habits. This fact was related to the emotional value, as indicated by the religious significance of dietary laws, with which the partaking of food is invested for Jewish mothers, even though many of the younger women do not adhere to the old practices. Various other aspects of the social and cultural life which leave their imprints on dietary habits were discussed by Remington.[60] If such a thing as dietary instinct exists, it would be characterized by the distrust for the unknown, for the things of unfamiliar taste, a distrust which is common to primitive man and animals. Food habits which have their origin in tribal life have been influenced in their development by numerous factors, such as religion, superstition, climate, industrial progress and advertising. A person forms his food likes and dislikes in early childhood, and he changes them under the influence of similar factors which operate for whole groups.

Hill [61] traced disorders in personality and disturbances in gastrointestinal dysfunction to the influence of early feeding experiences. He observed that some families showed more than usual interest in the condition of the upper part of the alimentary tract and in the things that pass through it. These families were proud of their good food, and their pleasure in eating was suggested by their obesity. They were fond of talking or singing. Some members of these families suffered from so-called digestive disorders, and some were alcoholic. He paid special attention to the management of breast feeding and concluded that either inadequate or excessive breast feeding was undesirable from both the physiologic and the psychologic point of view. Levy [62] studied the relation of maternal attitude to the early feeding histories in greater detail. In addition, he conducted animal experiments [63] in which he observed that puppies which had been subjected to irregularities of early feeding had different dispositions from those which were suckled for the usual time. Conrad's paper [64] on attitudes toward food deals with a number of patients who exhibited feeding difficulties during hospitalization for various somatic disorders. She was able to demonstrate

59. Hall, D. E.: Health Habits, Am. J. Orthopsychiat. **8**:618, 1938

60. Remington, R. E.: The Social Origin of Dietary Habits, Scient. Monthly **43**:193, 1936.

61. Hill, J.: Infant Feeding and Personality Disorders: A Study of Early Feeding in Its Relation to Emotional and Digestive Disorders, Psychiatric Quart. **11**:356, 1937.

62. Levy, D. M.: Maternal Overprotection and Rejection, Arch. Neurol. & Psychiat. **25**:886 (April) 1931; Maternal Overprotection, Psychiatry **1**:561, 1938; **2**:99, 1939.

63. Levy, D. M.: Experiments on the Sucking Reflex and Social Behavior of Dogs, Am. J. Orthopsychiat. **4**:203, 1934.

64. Conrad, A.: The Attitude Toward Food, Am. J. Orthopsychiat. **7**:360, 1937.

that in each case refusal of food or excessive or specific demands were an expression of the personal need and emotional maturation of the individual patient. Alexander,[65] basing his work on psychoanalytic concepts, established that the wish to be fed was, in the subconscious, identical with the wish to be taken care of, to be helped and to be loved.

PERSONAL OBSERVATIONS

Material.—The investigation into the food intake was aimed at an understanding of its origin and significance in the life of obese children. The mother, as the food giver, will greatly influence the attitude of the patient. I therefore not only studied the life history of the child, with his social and emotional reactions and adjustment, but probed into the origin of the mother's attitude as well. Such detailed life histories were obtained for 40 children and their mothers. In another large group of children, more information about the psychologic aspects of their development was obtained than is generally recorded in medical histories. As much information about the personality of the fathers and other members of the household was collected as was possible. A considerable amount of information has accumulated, and this will be published in detail at a later date after the physical and emotional development of some of the patients has been followed beyond puberty.[66]

This paper shall be restricted to a discussion of some of the general connections into which I have gained insight and to illustration of them by a few individual cases.

Emotional Immaturity and Overprotection.—Some of the problems to be dealt with have been mentioned earlier. The exaggerated expectation of the parents with regard to the amount of food which they considered necessary for the proper growth and health of their children has been discussed. The one-sided composition of the diet pointed to defects in training and to a persistence of the tastes of a more primitive level, with a rejection of all new foods. In her studies on self selection of diets by newly weaned children, Davis [67] observed that children who liked only a strictly limited number of foodstuffs learned later to eat others as a matter of social conformity and convenience. Lack of social maturation is an outstanding feature in the development of all obese children and manifests itself in many other ways. Many children are not capable of dressing themselves or of any other self care at an

65. Alexander, F.: The Influence of Psychologic Factors upon Gastro-Intestinal Disturbances: A Symposium, Psychoanalyt. Quart. **3**:501, 1934.

66. Bruch, H., and Touraine, G.: The Family Frame of Obese Children, to be published.

67. Davis, C. M.: Feeding After the First Year, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1938, vol. 1, chap. 30.

advanced age. It is not unusual to hear that a child of 10 years or more is still being dressed and bathed by his mother, is accompanied to school and is not allowed to play with other children. For such children, deprived of normal outlets and satisfying contacts, the activity and pleasure of eating gain inordinate importance, and such statements of mothers as "His heart goes out for food" or "Eating is all he thinks of and lives for" describe the situation. Yet this strong attachment to food is not something that has suddenly befallen the child; it can always be traced to experiences in early life.

The immature behavior of many of these children closely resembles that described by Levy [62] as resulting from maternal overprotection. This maternal attitude is obviously present in many instances, although often not in the form which Levy described as "pure" maternal overprotection.

Family Position of Obese Children.—One factor which may help to explain the long-continued overprotection is to be found in the unusual family position of these children. Fifty children (35 per cent) were only children, and 50 others (35 per cent) were youngest in their family; many children of the latter group were separated by five to twelve years from the next older sibling, thus being exposed not only to the excessive care of elderly parents but also to spoiling by older siblings. In 32 instances (22.5 per cent) the patient was the oldest child, frequently in a two child family in which the second child was more than five years younger, so that the patient had been in the position of an only child during a period of life when many important attitudes are formed. Only 10 obese children (7.5 per cent) had 1 or more older and younger siblings. Here again the factor of a large difference in age exposed some children to overprotection. In 3 of these cases the attitude toward the obese child had been influenced by the death of the preceding or succeeding sibling.

One boy seemed to be the exception to the rule with regard to his place in the family constellation; he was the third of 5 children, the age differences were not excessive and all the children were educated to assume their share of the responsibility in the home. The question concerning any possible difference in the early childhood of this patient was answered by the mother: "He was the baby twice." This statement was made only after I knew the family well, more than a year after the first contact. For some reason, apparently not a deliberate withholding of information, the mother had never mentioned that she had lost a child. The patient was the third boy, and the parents had been disappointed in their desire for a girl. The following child, only 14 months younger, was a girl. She died of an acute disease at 4 months of age. Anorexia and intestinal disorder were conspicuous symptoms

during the fatal disease of this child. For this reason, attention to food intake and digestion found exaggerated expression during the "second babyhood" of the patient.

Situations of this type were observed in a number of cases in which the common identification of good appetite with good health was overemphasized, and such situations often explained the unwillingness of the parents to interfere with the excessive food intake of their children. One mother, who had lost her first two children and whose oldest living child at the age of 11 was monstrously fat, still recounted with pride and a sparkle in her eyes how her neighbors had envied her her pretty baby with dimples in her cheeks. "They thought I gave her gold and diamonds to eat," she boasted.

Influence of Upsetting Experiences.—Not all the children had been obese from infancy. Frequently the increased desire for food became manifest only after some upsetting experience. The following case is particularly pertinent:

The patient was extremely overweight when he was first seen at 11¼ years of age. He was 57 inches (144.8 cm.) tall and weighed 150 pounds (68 Kg.); that is, he was 70 pounds (31.8 Kg.), or 84 per cent, overweight. The course of the boy's physical development is illustrated by figure 3. The weight curve has been constructed from figures which the mother had kept and from the clinic's record. His mother grew fat during pregnancy and had gained another 100 pounds (45.4 Kg.) since the patient's birth. The patient weighed 11 pounds (4,990 Gm.) at birth (the highest birth weight in my series). Throughout his childhood, he was heavier and presumably taller than the average child of his age; the figures for normal height and weight[19] are indicated by the interrupted lines on the chart. There was a sudden increase in weight after an appendectomy when he was 8½ years old. When he was 9 years old, the obesity had increased to such a degree that he was sent for treatment to the endocrine clinic, after admission to the hospital for pneumonia. His condition was diagnosed as hypopituitary obesity, and he was treated orally with whole pituitary and thyroid extracts. In addition, a low caloric diet was prescribed. He attended the endocrine clinic for five months, his weight remaining constant during this period. During the next year he followed the prescribed diet without further glandular treatment and showed no increase in weight. In the summer of 1936, when he was 11 years old, another sudden increase in weight occurred. In March of the following year he was first seen in the obesity clinic. Except for obesity, no gross anomaly was found on physical examination. Several laboratory examinations which were carried out did not add any relevant information. The subsequent course after dietary restriction was demonstrated by a decrease in weight during the next few months. During this time signs of pubertal development appeared, and the boy's pubertal age, if the appearance of axillary hair is used as an index of attained puberty, was 12¼ years.

In figure 3 there is a second normal weight curve (weight maturity 13 yrs.), which represents the weights of boys maturing at or before 13 years and which is taken from the study of Richey.[20] The weight curve of my patient, if one

disregards the sudden increases in weight, runs fairly close to this normal weight curve, which corresponds better to his biologic maturation. The changes in the appearance of this patient have been illustrated in a previous publication.[68]

The feeding history of this boy was characterized by the mother as offering "no difficulties." The mother could not nurse him, and he was entirely bottle fed. It was difficult to wean him from the bottle; until he was over 3 years of age he cried for it and would not go to sleep without it. After he had been forcibly weaned, he began to chew on whatever came into his hands. Frequently he chewed on wood. The mother used all kinds of threats to break this habit. She warned him that he might get sick and have to go to the hospital to have the wood cut out and that he might die as a result. Despite this threat, the boy did not break the habit until he was 8 years old, when an appendectomy was performed after an attack of acute abdominal pain. Nothing pathologic was found at operation; the mother, however, told him that the doctors had found a "terrible

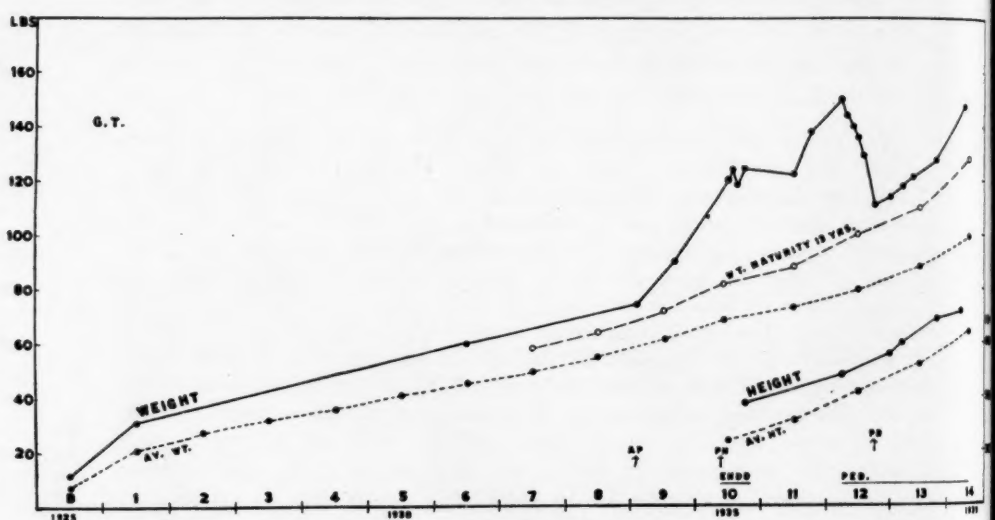

Fig. 3.—Chart showing the weight development of G. T., born June 1925. *Av. wt.* and *av. ht.* indicate average weight and average height. *Wt. maturity 13 yrs.* represents the weight curve for boys maturing at or before 13 years. The three arrows indicate the time of an appendectomy (*ap*), pneumonia (*pn*) and puberty (*pb*). *Endo* represents the period of treatment in the Endocrine Clinic, and *ped* the period of observation in the Pediatric Obesity Clinic.

mess of wood" inside him, that he nearly died of the operation and that he would have to go back for another operation if he did not stop chewing wood. The boy was so thoroughly frightened that he stopped the habit. However, his appetite became enormous, and he ate large quantities of bread and other starchy food.

This explains the first period of rapid gain in weight after the appendectomy. Without this detailed history one might speculate what physiologic relation could exist between hospitalization for an operation and subsequent gain in weight.

68. Bruch, [18] fig. 12.

This combination is not unusual in the histories of obese children. Frequently it is a tonsillectomy which gives the first hospital and operative experience. It was demonstrated with a large number of other patients that fear of the whole procedure, which is often used as a threat by parents, is directly connected with increased food intake.

The second period of excessive increase in weight, which appeared when this boy was 11 years old, occurred during a period when there was no fear of immediate danger to his health or life but after he had been led to fear that his development would be abnormal. After he had discontinued treatment in the endocrine clinic he followed the prescribed diet for several more months and did not gain in weight. He grew irritable and nervous during that period and started to bite his finger nails and chew on his hair. On the first day of the summer vacation he went down to play in the street, wearing a low-cut shirt and short pants. The other boys made fun of him because he was so fat and especially because he had "breasts," and they advised him to buy a brassiere. One older boy, whom he liked a good deal at the time, told him that he was not a normal boy, that he would develop like a woman and never be a real man. He felt so humiliated and was so convinced that he was abnormal that he completely withdrew. Throughout the summer vacation and all winter he kept much to himself, grew more nervous and irritable, was easily hurt and cried readily. His school work became poor. His chief occupations were to listen to the radio and to eat constantly. He consumed more than a loaf of bread a day, in addition to large amounts at mealtimes. The caloric intake was estimated to have ranged between 4,000 and 5,000 calories. He was so ashamed of his condition that he did not even want to go to the clinic. The mother literally dragged him into the examining room, calling him a "cry baby" and complaining that he did not behave like a real boy.

The patient and his mother were reassured regarding his sexual development. The fact that he lost 39 pounds (17.7 Kg.) during the next six months on a restricted diet of 1,500 calories and underwent early puberty without specific hormonal treatment is evidence in favor of the assumption that fear for the integrity of his body and not a deranged glandular system had caused the inordinate desire for food. The boy was encouraged to become more independent of his mother and to join other boys in their games and outdoor activities. The mother was not seen again for nine months. Her only complaint after that time was that he had "such grown-up ideas."

In a large number of other cases the fear of sexual maldevelopment had similar effects. Unlike this case, in which a playmate gave the enlightening information, in the majority of cases a physician, a school nurse or some other person in authority had warned the parents about the poor prognosis for spontaneous development. In a number of cases the diagnosis of sexual underdevelopment had been made even after secondary sexual characteristics had made their appearance at an early age. Generally several weeks or months of unhappiness and conflict had followed the information. The patients, already overweight, feared that something essential in their physical condition was wrong or was being neglected, and they resorted to eating, their usual way of seeking comfort. The ensuing rapid increase in weight was sometimes considered additional evidence that the glandular system was disturbed.

In other cases eating was used as a form of sublimating aggressive tendencies.

A 6 year old girl who was 16 pounds (7.3 Kg.) or 35 per cent overweight had begun to gain weight excessively when she was 3 years old, shortly after a younger brother had been born. When the baby was a few weeks old, the girl had been exposed to pertussis. To protect the infant from possible infection the girl was sent away to stay with relatives. After her return home her behavior had changed greatly. She had periods of great excitability, restlessness and insatiable appetite. She was so aggressive toward the younger brother that the mother would not leave the two children alone. The mother was requested to keep a daily record of the child's behavior, food intake and weight for a few weeks. During one week of poor behavior the child gained 6 pounds (2.7 Kg.). She lost some weight during the ensuing period of quiet, withdrawn behavior.

These instances exemplify only a few of the situations which gave rise to increased dissatisfaction, fear or aggressiveness which the children tried to appease by increased intake of food. Common to all children who reacted in this way was the inability to express themselves by constructive activities or to find an outlet in satisfying relations.

Origin of Mothers' Attitude Toward Obesity.—Only a few of the factors which helped to shape the parent's attitude will be mentioned. Many of them were immigrants who had experienced poverty and cruel hunger during their own childhood. Giving food in abundance to their children represented to them something more than appeasement of a bodily need. It also meant the safety of a peaceful country, the fulfilment of longings of their own which had been denied to them when they were younger. The grandmother of one of my patients, a Polish Jewess, had been killed by soldiers while she was trying to buy some food from a farmer. Her daughter, the mother of my patient, was left in great poverty. An Italian woman, when asked about obesity in her family, shrugged her shoulders, saying: "We were too poor to be fat, we always were hungry." To such mothers it is inconceivable that they should train their children to restrict food intake. "Why not give it to him when he wants it and there is plenty?"

The special emotional significance of food to Jewish mothers has been stressed by Hall.[59] The high incidence of obesity in Jewish children (more than 40 per cent of the patients in our group are Jewish) is in agreement with this observation. However, mothers of non-Jewish obese children valued food just as highly. I was not able to discover differences in this respect. To all of them food stood for more than its caloric value; it represented health and security and, more often, love and affection.

Prenatal Attitude of Mothers.—The need to display their love so obviously or bid for their children's affection by bribing them with food arose in some of these mothers from feelings of guilt toward a child who had been unwanted or from self accusation of having neglected

another child who had died. In more than half of the cases in which inquiry was made into the antepartum attitude of the mother toward the child, the information was given that the pregnancy had not been wanted. Several mothers admitted to having attempted abortion or had induced abortions preceding and following the pregnancy with the child that had become obese. Statements such as "I got caught" or "just an accident" were frequent. One mother crudely stated, "I nearly killed myself trying to get rid of him"; but she hastened to add, "After he was born we all were crazy about him. . . . I could never deny him a thing." This was one of the children who was more than 10 years younger than his next older sibling.

Early Feeding.—According to Levy [62] and others, the early feeding history frequently reflects the maternal attitude toward the child. I analyzed my records from this point of view. Information about breast feeding was recorded for 118 children (62 girls and 56 boys). Prolonged breast feeding, twelve to twenty-four months, was observed in 15 instances (12.5 per cent). This figure is low when compared with the number of Levy's cases of pure maternal overprotection. In his group of 20 overprotected children breast feeding was prolonged beyond the usual time in 10 instances. The significance of my figure is further diminished by the circumstance that with 2 exceptions in all cases observed the children were of South European or Negro extraction. The cases seem to represent more an adherence to national customs than an expression of an individual attitude.

Inadequate breast feeding, nursing less than 6 weeks, was recorded for 37 children (31.5 per cent). This is a high figure, especially in view of the fact that other aspects of the child's care had been obviously exaggerated. It is in agreement with the observation quoted by Levy in instances of "guilt overprotection" in which evidence of rejection is present besides overprotective features, a relation which appeared to be the one most frequently encountered in families of obese children.

My records are incomplete concerning the duration of bottle feeding. For the group of 40 children who were studied more intensively it was recorded fifteen times (38 per cent) that milk, soups and other fluids had been given by bottle beyond the first year. In these cases bottle feeding was generally extended to two or three years, in several instances beyond five years. The majority of the children who were bottle fed too long had had either no breast feeding or too little.

The manifestations of the maternal attitude and child-parent relationship varied widely from case to case. In all cases food represented an important tie between mother and child. To many of these mothers the offering of food represented the only way of expressing their devotion, and the child received what he wanted and what his need for satisfaction and security endowed with high value. From this point of view

of social and emotional adjustment such one-sided development is undesirable. In this sense the excessive weight indicates danger; it is the sign of an underlying disturbance, involving not one gland or organ system, but expressed by poor adjustment to the environment and by retardation in emotional maturation.

COMMENT

It was stressed in the beginning of this paper that food would be dealt with as one factor which is effective in the pathogenesis of obesity only in cooperation with other factors, which, however, have been deliberately disregarded. All the facts relating to food intake presented in this paper cannot be considered as the cause of obesity; they are, however, contributing factors which were found with such regularity in the history of obese children that they deserve to be looked on as of more than accidental occurrence and may be considered as having a specific significance. That identical or similar constellations are found in families whose children do not become obese but show other signs of maladjustment does not contradict this conclusion. Life situations and emotional experiences of this kind provoke increased desire for food only in a certain type of person and result in obesity only when such a person has a special tendency to store fat in larger amounts than others and does not increase the energy expenditure correspondingly. One may describe such a person as a representative of a special "constitutional" type. It is possible that experiences in early life condition a genetically predisposed person to such a way of reaction.

If one assumes that certain emotional experiences evoke an increased desire for food by hypothalamic stimulation, it is not inconceivable that the same experiences simultaneously act on the trophic centers, which in turn influence fat storage.[69] To gain further insight into the problem of obesity, it would be necessary for one to study the significance of fat storage and of body size in the individual. This problem, however, is beyond the scope of the present publication.

III. TREATMENT OF OBESITY BY DIETARY RESTRICTION

REVIEW OF THE LITERATURE

Since the excessive weight of the obese patient has resulted from excessive intake of food, restriction of the caloric intake below the energy requirements will result in a reduction of weight. Numerous reports[70] dealing with this problem have demonstrated convincingly that undernutrition results regularly in a predictable loss of weight.

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69. Hausberger.[38] Beznák and Hasch.[39]

70. Newburgh and Johnston.[2] Evans and Strang.[5a] Kenyon.[5b] Short.[5c] Murray, Dunlop and Lyon.[6] Lambie.[7] Campbell.[8]

There is general agreement that the success of a reducing regimen depends largely on the cooperation of the patient. Much has been said in general terms about the reasons why some patients cooperate and others do not. Unwillingness to break a habit and expectation that some drug will make the accumulation of fat disappear are the most frequently mentioned. Newburgh,[53] Campbell,[8] Hochman[56] and others emphasized that the relation between patient and physician and an understanding of the patient's problems are important in the successful management of weight reduction.

Circumstances are different in private practice and under the conditions of a dispensary. The patient who consults a private physician with the intention of losing weight will, as a rule, cooperate better[5] than a patient who attends a clinic for some disability, is sent from one department of a clinic to another and finally receives instruction for a low caloric diet because overweight is considered to be the cause of his complaints. Hunter[71] reported that of 2,447 patients referred to the dietetic department of the London Hospital for gross overweight, only 682 (27.5 per cent) attended long enough to be benefited. Of those who went regularly, 93 per cent were obedient and lost weight. A study which analyzes in detail the factor determining the cooperation of obese patients was not found in the literature.

PERSONAL OBSERVATIONS

The obesity clinic where I collected my information was conducted as a research clinic for study of the "natural history" of obesity in a large group of children. Much time and attention was given to the patients and parents who did not show good cooperation.

Regularity of Attendance.—Classification of patients according to the degree of cooperation involves subjective judgment of many factors. In an attempt to use an objectively comparable standard, I chose regularity of attendance as an index of cooperation. Although these two frequently fail to coincide, in the majority of cases regular attendance indicated at least the willingness of the patient to receive advice and to follow it as far as possible. Even in the group called "cooperative," no patient kept all appointments that were made for him. Patients whose visits to the clinic were more than twice as numerous as their broken appointments were counted as "cooperative." The patients classed as "uncooperative" reappeared only after repeated follow-up letters or after a visit of a social service worker to the home. In a few instances even a home visit did not induce the patient to return to the clinic for examination. In these cases information about the subsequent course is based on the observation made at the time of the home visits. Another group of patients returned to the clinic only for treatment of

71. Hunter, D.: Causes and Treatment of Obesity, Lancet **2**:1237, 1937.

other disorders. Patients who could not be followed or who had been seen only once or twice when this review was written were counted uncooperative; 37 patients fell into this group. A few of these were financially ineligible for clinic care and therefore could not be followed.

Since this division into "cooperative" and "uncooperative" patients could not be made on an entirely objective basis, the figures are presented with some reserve. Their arrangement in tables serves only for demonstration of certain trends.

The patients were grouped according to the reasons that had brought them to the Vanderbilt Clinic. Throughout the period of this study obese children were referred to the obesity clinic from other departments. This cooperation enabled me to gather information on obese patients who had sought medical advice not primarily for treatment of their obesity.

The relation between the reason for attendance at the clinic and subsequent cooperation is demonstrated in table 2. The smallest group is represented by the patients who had come spontaneously to the clinic for treatment of their obesity. This group of only 8 patients (5.6 per cent) showed the highest degree of cooperation; 1 patient who was ineligible for clinic care could not be followed and is therefore not counted among the cooperative patients. The degree of cooperation of this group (column 3 divided by column 1 in table 2) is 87.5 per cent. Thirteen patients had been referred for treatment from other clinics (fracture, dermatologic, psychiatric, etc.). This group ranges in second place regarding cooperation. The school (or health station, in the case of younger children) had been concerned about the obesity of 33 children and had advised them to apply for clinic care. Forty per cent of them showed interest in treatment.

Twenty-six (48 per cent) of 54 patients in these three groups (38 per cent of the total number) were cooperative. More than half the patients discontinued treatment before the condition was corrected, even though they had been sent to the clinic because they were overweight.

The other 88 patients (62 per cent) had not presented themselves for treatment of obesity, though it was sometimes mentioned as an additional complaint and was generally the outstanding clinical symptom. The children whose reason for attendance at the clinic was listed as "endocrine disorder" comprised those who were referred with a definite diagnosis of glandular disorder; a diagnosis of sexual maldevelopment had been made in the majority of instances. The assumption that obesity is an expression of glandular disorder is so prevalent that a question concerning the condition of the endocrine glands was raised in nearly every case. The children in this group came for the definite purpose of receiving injections, which, in my opinion, were not indicated in most instances. This group showed the poorest cooperation.

Many parents declared: "If it is not the glands, I don't care if he is stout." Some patients insisted on receiving injections and refused to follow advice in other respects.

The children who came to the clinic because of "behavior disturbances or enuresis" included those who complained about anxiety attacks, fatigue, poor work in school, restlessness and similar disturbances or of enuresis for which no organic basis could be discovered. A third of the patients of this group attended the clinic fairly regularly.

The remaining 44 patients (31 per cent) had applied for treatment at the pediatric clinic for various somatic complaints, ranging from common colds and acute infections to vomiting attacks, facial paralysis and pneumonia. A number of them had come for tonsillectomy and discontinued treatment after the operation had been performed. Approxi-

TABLE 2.—*Reason for Clinic Attendance in Relation to Subsequent Cooperation of Obese Children*

Reason for Clinic Attendance	1 Number of Patients	2 Percentage of Total	3 Number Cooperating	4 Percentage of Cooperation
Obesity (spontaneous attendance)	8	5.6	7	87.5
Obesity (sent from other clinics)	13	9.2	6	46.0
Obesity (sent by school)	33	23.2	13	40.0
Endocrine disorder	23	16.2	6	26.0
Behavior disturbance or enuresis	21	14.8	7	33.3
Acute disorder	44	31.0	12	27.0
Total	142	100.0	51	36.0

mately a quarter of these patients showed continued interest in a correction of the obesity.

There was a definite increase in the degree of cooperation with the severity of the condition, as is illustrated by table 3. Only a small number of the patients who were moderately overweight were interested enough in reducing to attend the clinic regularly. Two thirds of the children who were more than 70 per cent overweight came regularly. The relation between cooperation, reason for attendance at the clinic and severity of obesity is demonstrated in table 4. Patients with different degrees of obesity had applied for treatment for various reasons. The extremely obese patients who did not cooperate as a whole showed little interest in reducing.

The main conclusion to be drawn from these figures is that obesity is a condition that per se rarely induces a patient to apply for treatment. In young children striking degrees of obesity escape the attention of the parents. The mother of a 3 year old girl of 70 pounds (31.8 Kg.) said that she had been sent by the health station because the child was

too fat. The mother added: "To me she does not look that way. Do you think she is too fat?" The appearance of the child is illustrated by figure 4. Many mothers of older children who were tremendously overweight claimed not to have recognized this until the school drew their attention to it and insisted on treatment. The subsequent course and lack of cooperation of many of these patients who came after repeated urging shows that even the knowledge that the child is too fat does not imply to the parent or the patient the need for a correction.

TABLE 3.—*Degree of Obesity in Relation to Cooperation of One Hundred and Forty-Two Obese Children*

Degree of Obesity	Number of Patients	Cooperative Patients		Uncooperative Patients	
		Number	Per Cent	Number	Per Cent
Moderate	66	19	29	47	71
Severe	61	22	36	39	64
Extreme	15	10	66.6	5	33.3

TABLE 4.—*Degree of Obesity in Relation to Reason for Clinic Attendance of One Hundred and Forty-Two Obese Children*

Degree of Obesity	For Obesity (Spontaneous Attendance)	For Obesity (Sent from Other Clinics)	For Obesity (Sent by School)	For Endocrine Disorder	For Behavior Disturbances or Enuresis	Acute Disorder
			Cooperative Patients			
Moderate	1	2	5	3	3	5
Severe	4	4	3	2	3	6
Extreme	2	..	5	1	1	1
			Uncooperative Patients			
Moderate	1	6	8	8	7	17
Severe	..	1	10	9	5	14
Extreme	..	..	2	..	2	1

One mother, who brought the patient to the clinic when the school insisted on it, expressed her own and the family's opinion: "The family thinks the bigger he is, the healthier he is." Although other parents expressed their opinions less clearly, a similar attitude was implied in many other ways. If obesity is not considered a sign of superior health, it is generally not thought of as abnormal. As long as the child eats large quantities of food, the parents are not worried about the progressive increase in weight.

Therapeutic Results.—The evaluation of the results of treating children with obesity meets with a number of difficulties. Since the children are growing in stature and undergo rapid changes in their biologic maturation, a report of the loss in weight or its percentage in

relation to height is not entirely representative. The previous course of the weight development has to be considered also. For a young child who has been gaining excessively during the preceding years, constancy of weight or normal rate of gain during the following years presents a satisfactory result. In older children whose weight is above that of fully grown normal adults, actual loss in weight is desirable. The same holds true for extremely obese children to whom the excessive weight is a handicap in physical activities and social relations. At present the number of patients in my group who have been followed for several years is too small to warrant an evaluation which includes these different factors. Such a report will be given at a later date. That a rigid adherence to a low caloric diet produces a loss in weight is a well established fact. The efficacy of any treatment of obesity can be appraised only by the permanence of the result.

Fig. 4.—T. S. at the age of 3 years and 1 month. Her height was 41 inches (104 cm.), her weight 70 pounds (31.8 Kg.).

A further difficulty in the evaluation of results in this group is presented by the inclusion of many uncooperative patients. The classification according to regularity of attendance served only to demonstrate that the complaint which had brought the patient to the clinic influenced his subsequent attitude toward treatment. Regularity of attendance does not mean that the patient followed my advice implicitly. These patients afforded me an opportunity to study the factors which had played a role in the development of the obesity and which interfered with restriction of the food intake. Even though the patients who came regularly did not, as a rule, follow dietary advice closely, the majority of them lost weight as long as they attended the clinic at frequent intervals.

The patients who were classified as "uncooperative" because they frequently broke their appointments did not entirely disregard instructions. They also lost weight, or else the rapid gain in weight became arrested, during the period when they kept their appointments. But the differences in the results were striking. Twenty-seven children who were classified as cooperative for a short period, six months or less, lost on the average 2.7 pounds (1.25 Kg.) per month. Seventeen children who were followed less than six months and were uncooperative lost on the average 0.14 pounds (0.07 Kg.) per month.

Differences became even more apparent in the children who were followed longer than six months. No child, whether or not he was cooperative, continued to lose weight at the same rate for a long period. The importance of the time factor for permanent results shows itself in the smaller number of patients who were cooperative over a long period. Twenty-four patients kept their appointments fairly regularly longer than six months. Thirty-seven patients, some of whom had been cooperative in the beginning, broke later appointments and were seen again, only after repeated requests or after a visit to the home or when they were referred again by the school. In the cooperative group the subsequent course was that of weight constancy or slow increase. In the uncooperative group all patients with a single exception gained during the intervening time, generally at a greater rate than normal children though often at lower rate than prior to their first visit to the clinic.

It is not intended at present to give detailed figures and reports of cases. The differences between the results in individual cases covered a wide range. As stated previously, the greatest losses in weight were observed in patients who were cooperative for a long period. Five lost over 20 pounds (9.1 Kg.) in weight during the first six months; the greatest loss in weight was 39 pounds (17.7 Kg.) in six months.

In patients who did not follow a diet for a longer period although they were interested in reducing, the effect of a gonadotropic substance

from the urine of pregnant women on appetite and weight were tested. In none of these cases was an influence on intake of food or loss of weight observed. One boy who presented a serious emotional disturbance and who lost weight during the first four months, as long as he was seen at two week intervals, began to gain again when his appointments were given less frequently. He received 2,000 units of a gonadotropic substance from the urine of pregnant women (follutein), two injections a week, but was not seen in interviews. The rate of gain in weight was no different during the period when he received injections from the rate when he was not treated. Another patient, whose increase in weight was not influenced by injections of follutein, lost satisfactorily on dietary restriction alone during a period of hospitalization.

COMMENT

My observations are in agreement with the reports of others that undernutrition results in loss of weight. The calculation of a low caloric diet which fulfils all the demands for adequate intake of protein, minerals and vitamins offers no difficulty. The real problem of treatment lies in the unwillingness or inability of the children to adhere to the prescribed diet. It is the task of the physician to gain the cooperation of the patients and their parents. The inquiry into the life history of the patients was undertaken with the aim of arriving at an understanding of their personal needs. The psychologic factors, some of which were discussed in the second part of this paper, help to explain why a change in the diet and eating habits frequently upsets a precarious balance in the relations between the patient and his parents. The exaggerated importance of food was discussed as having resulted from experiences and attitudes which were closely connected with the whole development of the person.

Since food intake is not an accidental isolated factor but plays an essential role not only for the physical needs but even more for the emotional demands of the patient, change in the dietary regimen should be accompanied or preceded by adjustment of other difficulties. The question has been raised repeatedly as to whether it is advisable to treat obese children by dietary restriction. Some authors feel that it is better to leave the children untreated, since they become nervous and irritable on a restricted diet. Solution to the problem lies in individual approach. No definite rules and fixed dietary regimens can overcome this difficulty; each patient has to be handled according to his personal needs.

It is preferable not to change the eating habits in cases in which the environmental conditions are unusually detrimental or in which the patient is emotionally so disturbed that psychiatric therapy is indicated. Two cases in my group represent this type. In one of them, a boy of 12½ years, whose behavior and character had changed con-

spicuously after the death of his father, was suspected of suffering from beginning schizophrenia. The patient was 50 per cent overweight. In view of the seriousness of his mental state, no dietary restriction was advised.

The patient in the other case was a boy of 11½ years who was 27 per cent overweight and who followed a diet with unusual faithfulness. It was observed that he had become more shy and withdrawn than when first seen. The father, who accompanied the patient to the clinic, gave evasive information. In an attempt to make contact with the mother, a visit to the home was made. It was discovered that the boy was living not with his parents but with his grandfather, who gave him instructions in Hebrew. The private studies, together with conscientious work on his school assignments, occupied the time not spent in school. The boy had never had any friends and had no opportunity for play or physical activities. The family was unapproachable for suggestions to change the situation. This patient had followed the dietary restriction with the same rigidity which his whole upbringing had imposed on him. In this case it was certainly a mistake to have added to the burden of restrictions and deprivations which pressed down on the patient.

Such cases are rare; these 2 were the only ones in my series. The other patients could have been treated successfully if they had continued to attend the clinic. Many patients failed to return to the clinic before a satisfactory contact or study could be made. In addition to lack of interest in the obesity, the conception that something on the somatic level was wrong and had to be treated was a frequent reason for discontinuance of the visits to the clinic. The parents generally had heard about certain types of treatments and expected them to be used for their children also. They were suspicious of an approach that differed from what frequently had been advised by some other physician. Only one mother expressed a definite objection to questions relating to her private affairs; this was the same mother who insisted on injections for the treatment of her boy and refused to accept any other advice. The majority of the mothers welcomed the opportunity to discuss their problems but were not willing to cooperate to effect a change.

No definite outline can be given for the diet which should be prescribed in individual cases. The caloric intake should always be lower than the amounts previously eaten. Frequently a reduction to the amounts generally recommended for normal children will be sufficient. With the exception of a few cases in which a rapid decrease in weight is desirable, the very low caloric diets which have been devised for adults [5] are not advisable for children. The caloric value of the diets which we prescribed ranged from 1,000 to 1,600 calories. The amount to be prescribed was determined by the previous food intake, the rate of gain and the expected cooperation of the patient. The protein content

varied from 60 to 80 Gm., according to the age and weight of the child. Attention was given to adequate intake of minerals and vitamins.

The reduction of the diet should not be so drastic as to impose on the child demands which are not within his power to follow. The child feels a sense of guilt over breaking his diet and fears to return to the clinic. In the majority of cases in which information was obtained as to why the appointments were broken, the child's inability to follow dietary advice was reported as the main cause. Either the children refused to return or the parents felt they were wasting time and money for advice which the child would not follow.

The cooperation of the family should be gained or the possibility for it assessed before any dietary advice is given. To request a record of the daily food inake for a week or two proved helpful for this purpose. The responsibility for keeping the record and for the honesty of the entries was given to the child, and the mother was requested not to remind the child about keeping the record or to interfere with his food intake during this week, even if he gained more weight. The manner in which this request was met was frequently indicative of the subsequent cooperation. Patients who forgot to keep these diaries were not interested in or were even antagonistic to any change. Mothers who made it a troublesome duty for the patient were likely to nag constantly about the diet and provoke the child to rebel against continuation of the treatment.

It was explained to the patient that the food diary was necessary if he was to be given a diet which considered his personal habits. As far as was compatible with the necessary caloric restriction, such individual considerations were given. Special instructions were given to children who had their lunch in school and for vacation periods and hikes. Although the instructions aim at a definite change in the previous habits, the diet must not raise a new barrier in the social relations of the child. In many cases it is advisable and necessary that the whole family change its eating habits.

Since most of the obese children had been overprotected and had not learned to take responsibilities, the dietary instructions were given as an inducement for the patient to prove that he could do something himself without supervision. It is not always possible to gain the cooperation of the mother for such a regimen. Many mothers who previously have not permitted their children to acquire independence and have not trusted them with the simplest self care cannot be persuaded to surrender their domination by giving up the close supervision of the child's food intake. In such cases the prescription of a diet provides a new battleground where the child controls his mother with temper tantrums related to food and the mother prevents the child from any cooperation by her constant interference.

In many cases of serious maladjustment, cooperation regarding diet cannot be expected before the underlying disturbance has been relieved. In no case should one restrict the diet without offering to help the child find some other outlet and satisfaction.

SUMMARY AND CONCLUSIONS

An inquiry into the eating habits of 142 obese children was made. Relevant information was obtained concerning 136.

The families of 80 per cent of the children had recognized that the food intake was larger than average. Attempts at reducing had already been made by 6 per cent.

The food intake of 20 per cent of the children was described as normal or small. In the cases in which a detailed study could be made the terms "normal" and "small" were an expression not so much of the food intake of the child but of the exaggerated expectations of the parents as to what their children should eat.

In all cases food intake was in better agreement with the rate of gain in weight than with the excess in weight.

The composition of the food showed a one-sided preponderance of starchy food, which was explained as perseveration on an infantile level of taste development.

Information concerning the emotional significance of food was obtained in the majority of cases. The emotional development of 40 of the patients and of their mothers was studied in detail.

The majority of the children had been exposed to prolonged overprotection, and they exhibited signs of immature behavior not only in their eating habits but in other respects. For many obese children deprived of other outlets and satisfying contacts, the intake of food had gained an inordinate importance.

The family position of many obese children partly explained the prolonged overprotection. Thirty-five per cent of the children were only children, and another 35 per cent were youngest children. In many instances a great difference in age or the death of another sibling had accentuated the peculiarity of the family position.

Increased desire for food and obesity frequently became manifest only after some upsetting experience. Two pertinent cases in which obesity developed at periods of fear for the integrity of the body and of suppressed aggression are reported in detail.

Some of the factors which helped to shape the maternal attitude are discussed. Deprivation during the mother's own childhood and rejection of the child were frequently observed.

The histories of the early feeding of the children disclosed a certain discrepancy. Breast feeding was inadequate for more than 30 per cent of the children, whereas bottle feeding was frequently prolonged.

In all instances the offering and receiving of food represented an important emotional tie in the mother-child relation.

The efficacy of dietary restriction depended largely on the cooperation of the patients and their families. The cooperation in my group was determined by the severity of the condition and the reason for attendance at the clinic.

Obesity was found to be a condition that per se rarely induced children to apply for treatment. Only 5.6 per cent of the patients came spontaneously for treatment of obesity. This group showed the best degree of cooperation. The poorest cooperation was shown by the children who came to the clinic with the definite expectation of receiving glandular injections for correction of the excess weight.

No definite dietary scheme is offered in this paper; several factors, however, which are of importance in the management of patients under dietary restriction are discussed.

The literature relating to the regulation of weight and food intake is reviewed. Experimental evidence and clinical observation point to the hypothalamic region as the site of the organic disturbance.

The hypothesis is advanced that emotional experiences call into play functional disturbances of the hypothalamus which may be of importance in the large group of obese patients in whom no organic lesion can be detected.

HYPOAMINOACIDEMIA IN CHILDREN WITH NEPHROTIC CRISES

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The failure of children with the nephrotic type of Bright's disease to regenerate plasma protein when fed a diet approximately optimal for the assimilation of nitrogen cannot be attributed solely to loss of protein in the urine in all cases; sometimes severe hypoalbuminemia occurs with but slight loss of urinary protein.[1] Further, rapid regeneration of plasma protein during recovery is, within wide limits, independent of the protein content of the diet.

In observing nephrotic children in this clinic we have also noted that acute febrile episodes with peritoneal symptoms were most frequent in patients with a plasma albumin content below 1 Gm. per hundred cubic centimeters. Sometimes these episodes were accompanied by pneumococcic bacteremia and peritonitis, but often an episode ran its course without such infection. It was suggested in a previous study that when bacterial invasion occurs it may be secondary to acute disturbances in metabolism which cause diminished resistance to infection rather than to a fresh infection.[1c] In favor of this hypothesis was the fact that in many instances the invading type of pneumococcus was recovered from the nasopharynx long before infection of the blood stream or the peritoneum occurred.[2] For the metabolic disturbance and clinical syndrome which seem to occur independently of infection, the term "nephrotic crisis" was suggested earlier.[1c]

We have sought for indications of metabolic changes in these crises and have found the most striking alteration in the concentration of amino acid in the plasma.

From the Hospital of the Rockefeller Institute for Medical Research.

1. Farr, L. E.: (*a*) Assimilation of Protein by Young Children with the Nephrotic Syndrome, Am. J. M. Sc. **195**:70 (Jan.) 1938; (*b*) II. Effect of Dietary Fat and Carbohydrate on Nitrogen Balance, Am. J. Dis. Child. **58**:935 (Nov.) 1939; (*c*) III. Effect of Nephrotic Crises on Assimilation of Nitrogen, ibid. **58**:939 (Nov.) 1939.

2. MacLeod, C. M., and Farr, L. E.: Relation of the Carrier State to Pneumococcus Peritonitis in Young Children with the Nephrotic Syndrome, Proc. Soc. Exper. Biol. & Med. **37**:556 (Dec.) 1937.

CONDITIONS OF OBSERVATION

All data were obtained on patients in the hospital under continuous observation. Throughout the period of observation there was no improvement in the characteristic nephrotic symptoms of 3 of the patients: G. B., aged 3½ years; J. C., aged 5½ years, and R. F., aged 13 years. One patient, J. T., aged 7 years, was rapidly recovering from his second attack of nephrosis and had been in the hospital for five months before this work was begun. The fifth patient, R. W., aged 7 years, had just recovered from an attack of acute hemorrhagic Bright's disease in which a marked nephrotic component had been present. The children were on constant weighed diets throughout the study. During the period of study, none of the children acquired an infection except J. T., who had a minor infection of the upper respiratory tract, from which he made a rapid recovery. J. C., G. B. and R. F. had nephrotic crises. At the time of the first elevation in temperature a blood culture was made, and blood cultures were made frequently during each febrile period. In every instance abdominal paracentesis was performed, and sufficient fluid was withdrawn for culture and study.

Blood for chemical analysis was drawn when the nephrotic crisis had subsided and after the patient had fasted overnight and had gone for at least two hours without fluids. During nephrotic crises the blood was obtained early in the morning but not after an overnight fast, as the patients were fed on a four hour schedule during these episodes. The bleeding was timed to follow a feeding at the maximum interval. To test the ability of these patients to absorb proteolytic products of digestion from the gastrointestinal tract, 2 patients, J. T. and J. C., were fed a single meal with a high protein content after an overnight fast. Each child received in this meal 2 Gm. of protein per kilogram of ideal body weight. J. C. ate 34 Gm. of protein and J. T. 43 Gm. Sufficient fat and carbohydrate were given to insure palatability. Each child required about fifteen minutes to eat the meal. Blood for chemical analysis was obtained during fasting and for three hours after eating, at intervals of forty-five minutes.

After the blood was withdrawn it was transferred with care to a flask containing an oxalate to prevent hemolysis. One portion was immediately centrifuged, and the plasma was removed as completely as possible without disturbing the packed cells. After removal of the plasma the centrifuged cells were laked in enough distilled water to make the volume of cell solution equal to the original volume of whole blood. Aliquots of plasma and cell solution were used for the determinations of amino acid nitrogen, which in most instances were completed within two hours after the withdrawal of the blood. The amounts of nonprotein nitrogen, albumin and globulin in the plasma were also determined. The urea and hemoglobin contents of the portion of whole blood which was not centrifuged were determined.

METHODS OF ANALYSIS

The amino nitrogen content of the plasma and of the cells was determined by both the Van Slyke nitrous acid method [3] and the MacFadyen and Van Slyke ninhydrin method.[4] The urea nitrogen content of the blood and urine was determined by the hypobromite technic of Van Slyke and Kugel,[5] and the plasma

3. Van Slyke, D. D.: Manometric Determination of Primary Amino Nitrogen and Its Application to Blood Analysis, J. Biol. Chem. **83**:425 (Aug.) 1929.

4. MacFayden, D. A., and Van Slyke, D. D.: Determination of Amino Acids in Blood and Urine by Their Reaction with Ninhydrin, to be published.

5. Van Slyke, D. D., and Kugel, V. H.: Improvements in Manometric Micro-Kjeldahl and Blood Urea Methods, J. Biol. Chem. **102**:489 (Oct.) 1933.

protein and nonprotein nitrogen contents were determined by the gasometric micro-Kjeldahl method of Van Slyke.[6] Hemoglobin estimations were carried out gasometrically by the oxygen capacity method of Van Slyke and Neill.[7] Howe's method was used for separation of plasma albumin and globulin.[8] The urea clearances were calculated by the formulas of Møller, McIntosh and Van Slyke,[9] in which the urine values included urinary ammonia. Van Slyke, Page, Hiller and Kirk[10] showed that in cases of nephritis the latter formulas give more consistent clearance values than do those formulas calculated from urinary urea without the ammonia.

RESULTS

The results of the chemical studies of blood in relation to nephrotic crises are given in detail in table 1 and chart 1. They show clearly that nephrotic children are subject to an acute disturbance of plasma amino acid regulation. This disturbance begins without clinical warning, and when not complicated by infection it appears to be self limited. All cultures of blood and ascitic fluid were sterile in the cases of acute illness here reported.

In each instance the acute illness which we have termed "nephrotic crisis" was accompanied by a sharp and sudden fall in the amino acid content of the plasma. We were unable to predict the time of onset of the crises because they began so abruptly. Therefore we were unable to obtain blood immediately before there were any clinical manifestations. We have, however, data on some patients twenty-four to forty-eight hours before the illness developed, and these data showed a plasma amino nitrogen value above 2.5 mg. per hundred cubic centimeters. Blood obtained at the time of the first clinical evidence of illness, namely, the rise in temperature, always showed a severe hypoaminoacidemia which persisted for the period of acute clinical illness, usually forty-eight to fifty-two hours. We obtained blood at the time when the temperature first returned to normal and found that the amino acids had returned to a level above 2.5 mg. of amino acid nitrogen per hundred cubic

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8. Howe, P. E.: The Determination of Proteins in Blood: A Micro Method, J. Biol. Chem. **49**:109 (Nov.) 1921.

9. Møller, E.; McIntosh, J. F., and Van Slyke, D. D.: Studies of Urea Excretion: II. Relationship Between Urine Volume and the Rate of Urea Excretion by Normal Adults, J. Clin. Investigation **6**:427 (Dec.) 1928.

10. Van Slyke, D. D.; Page, I. H.; Hiller, A., and Kirk, E.: Studies of Urea Excretion: IX. Comparison of Urea Clearances Calculated from the Excretion of Urea, of Urea Plus Ammonia, and of Nitrogen Determinable by Hypobromite, J. Clin. Investigation **14**:901 (Nov.) 1935.

TABLE 1.—*Detailed Data on Blood Chemistry of Nephrotic Children, Showing Relation and Lack of it Between Various Plasma Constituents During Nephrotic Crises and on Recovery from Nephrotic Syndrome*

Patient, Sex, Age	Date	Plasma Amino Nitrogen (Nitrous Acid Method) Mg. per 100 Cc.	Plasma Amino Nitrogen (Ninhydrin Method) Mg. per 100 Cc.	Plasma Nonprotein Nitrogen, Mg. per 100 Cc.	Whole Blood Urea Nitrogen, Mg. per 100 Cc.	Plasma Albumin, Gm. per 100 Cc.	Plasma Globulin, Gm. per 100 Cc.	Total Plasma Protein, Gm. per 100 Cc.	Hemoglobin, Volume per Cent	Cell Amino Nitrogen (Nitrous Acid Method) Mg. per 100 Cc.	Cell Amino Nitrogen (Ninhydrin Method) Mg. per 100 Cc.	Urea Clearance, per Cent of Normal
J. C.	3/ 1	3.45	2.74	17.0	7.5	0.63	3.23	3.86	20.2	.....	.....	98
♂	3/ 8	4.12	3.09	25.0	12.0	1.41	3.01	4.44	19.5	.....	.....	..
5½ yr.	3/15	3.56	2.80	20.3	10.9	1.22	3.06	4.28	20.8	.....	.....	90
	3/22	3.69	2.92	22.0	8.6	1.28	3.30	4.58	19.0	10.83	6.39	102
	3/24	2.13	2.04	29.0	12.6	1.04	3.16	4.20	19.2	19.87	22.48	122
	3/25	2.58	2.16	25.9	9.9	0.61	3.23	3.84	18.3	15.93	32.99	84
	3/26	2.95	2.10	25.6	8.6	0.36	4.06	4.36	16.8	12.41	19.31	108
	3/28	4.36	3.09	35.5	6.6	0.86	3.65	4.51	16.3	9.84	11.50	...
	4/ 5	3.58	3.09	13.8	10.2	1.14	3.20	4.34	18.1	10.61	10.41	75
	4/12	3.85	3.09	17.9	7.9	1.55	2.63	4.18	18.6	11.15	6.00	83
	4/18	3.87	3.15	12.3	7.6	1.16	2.79	3.95	18.6	11.82	11.45	100
	4/25	3.26	2.74	22.8	10.3	1.08	2.93	4.01	19.4	10.66	.....	66
	5/ 3	2.44	2.27	15.1	9.1	0.81	3.04	3.85	19.2	13.60	.....	61
	5/ 9	3.44	2.57	....	10.0	0.78	3.39	4.17	18.4	14.19	.....	76
	5/10	2.18	2.10	....	8.4	....	....	....	....	10.45	.....	63
	5/11	2.56	2.16	....	15.7	....	. ..	....	....	11.67	.....	46
	5/12	4.55	1.92	....	6.4	....	....	....	....	10.57	.....	137
	5/13	4.20	3.03	....	19.8	....	....	....	....	7.82	.....	47
	5/17	4.01	....	....	6.5	1.53	3.06	4.59	14.7	12.35	.....	86
	5/23	4.31	3.67	....	11.1	1.76	3.11	4.87	17.0	9.55	.....	77
	5/25	4.32	3.62	....	12.2	....	....	....	17.1	11.12	.....	..
	5/30	3.77	3.27	....	10.6	0.78	2.68	3.46	17.9	11.86	.....	46
	6/ 6	3.92	....	20.5	8.4	1.33	2.85	4.18	17.5	13.32	.....	48
	6/13	4.53	....	22.4	8.7	1.57	2.75	4.32	18.6	14.75	.. ..	69
	6/20	4.36	....	12.1	8.8	1.43	2.83	4.26	17.4	14.74	.. ..	67
R. F.	6/10	4.53	2.97	31.0	21.7	1.68	2.36	4.04	....	.....	.....	63
♀	6/11 a.m.	3.76	2.39	35.7	29.3	1.38	2.61	3.99	10.6	18.13	.....	29
13 yr.	6/11 p.m.	3.33	2.57	55.3	36.1	1.42	2.54	3.96	....	19.91	.....	18
	6/12	3.90	2.80	66.3	42.0	1.34	2.82	4.16	11.3	15.53	.....	19
	6/13	3.74	2.97	68.1	46.0	1.53	2.98	4.51	11.3	17.38	.....	20
	6/14	4.88	3.67	....	41.8	....	....	....	....	.....	.....	22
	6/22	5.72	....	35.4	18.8	2.64	2.76	5.40	14.8	17.46	.....	39
J. T.	3/ 1	2.97	2.51	20.0	7.5	0.73	3.04	4.07	17.1	.....	.....	132
♂	3/ 8	3.90	2.80	21.0	14.1	1.63	2.82	4.45	16.3	.....	.....	...
7 yr.	3/15	4.48	3.38	17.3	8.0	2.53	2.50	5.03	17.1	.....	.....	105
	3/22	3.40	3.33	16.1	8.7	3.03	2.70	5.73	17.9	11.11	6.06	141
	4/ 5	3.65	3.73	12.2	7.5	2.41	2.35	4.76	17.7	11.00	6.55	86
	4/12	3.80	3.62	21.8	7.3	3.03	2.34	5.37	17.5	11.17	.....	109
	4/18	3.98	3.62	13.5	6.5	2.88	2.08	4.96	17.5	9.29	9.55	130
	4/25	3.70	3.38	18.4	14.9	1.43	2.77	4.20	17.7	10.40	.....	131
	5/ 3	3.58	3.09	18.4	9.7	2.29	2.68	4.97	17.7	10.43	.....	119
	5/ 9	4.08	3.85	....	9.0	2.95	2.28	5.23	18.2	11.53	.....	121
	5/17	4.35	3.91	....	7.9	3.36	2.07	5.43	17.9	11.36	.....	137
	5/23	4.40	3.80	....	8.3	3.29	2.05	5.34	18.0	10.66	.....	119
	5/25	4.49	4.03	....	....	....	....	....	....	11.23	.....	...
	5/30	4.05	3.91	....	9.6	3.61	2.05	5.66	18.7	9.91	.....	140
	6/ 6	4.93	4.03	18.5	8.6	3.47	1.93	5.40	17.9	11.00	.....	145
	6/13	4.41	....	19.5	10.1	3.30	1.99	5.29	17.9	12.53	.....	128
	6/20	4.83	....	18.0	8.1	3.07	2.27	5.34	17.9	12.66	.....	143
G. B.	4/12	3.21	2.16	22.9	....	0.90	2.90	3.80	19.2	15.58	9.87	...
♀	4/14	3.96	2.68	23.5	18.2	1.09	2.83	3.92	16.8	12.66	8.72	49
3½ yr.	4/25	3.69	3.09	25.9	10.0	1.02	3.13	4.15	17.1	16.67	.....	67
	5/ 9	3.90	4.08	....	8.1	1.48	2.94	4.42	17.4	14.18	.....	137
	5/23	4.51	...	....	9.6	0.98	2.76	3.74	17.8	12.08	.....	92
	6/ 6	4.01	....	20.6	8.0	1.25	2.91	4.16	16.7	13.72	.....	94
	6/20	4.66	....	11.0	9.1	0.73	3.09	3.82	15.4	18.81	.....	108
R. W.	4/25	3.65	4.20	22.9	10.8	4.50	2.57	7.07	17.9	10.11	.....	73
♂	5/ 9	3.73	4.15	....	10.2	4.52	2.34	6.86	17.5	12.36	.....	108
7 yr.	5/16	4.14	3.73	....	8.7	4.40	2.47	6.87	17.8	10.28	.....	127

centimeters of plasma. The sharp onset and critical recovery together with the absence of any prodromal fever are shown by the characteristic temperature curves in chart 2.

Characteristic and constant changes in the urea clearance were lacking. In some instances the clearance was unchanged but in general, with the excessive prostration the clearance decreased, rising again with recovery. The effects on renal function were entirely transitory and

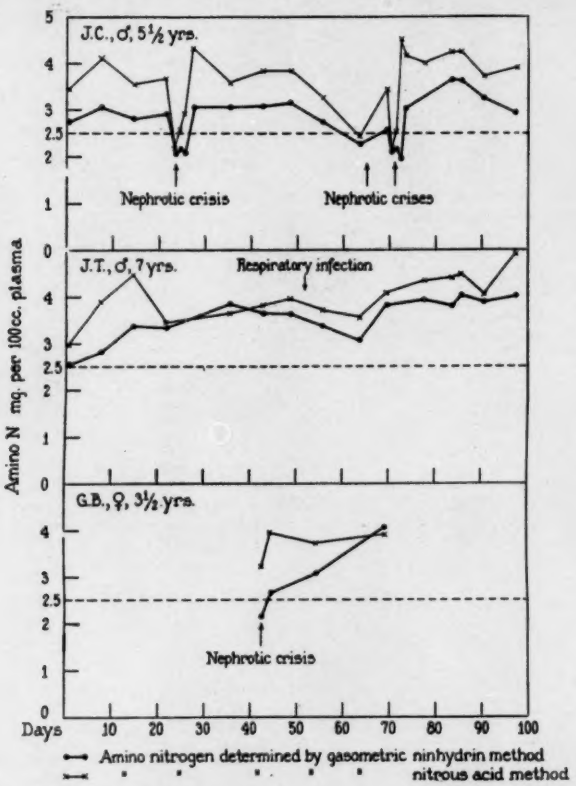

Chart 1.—Graphic summary of the plasma amino nitrogen level determined by two methods, showing changes before, during and subsequent to, nephrotic crises in J. C. and G. B. The gradual increase in plasma amino nitrogen during recovery is shown in the graph for J. T. Clinical symptoms are not manifest when the plasma amino nitrogen exceeds 2.5 mg. per hundred cubic centimeters as determined by the ninhydrin method. The normal value by this method probably exceeds 4 mg. per hundred cubic centimeters.

of the nature of the changes seen after fatiguing exercise. The attacks did not appear to affect materially the renal lesion.

In most cases the significant physical findings were limited to the abdomen, the skin and the general appearance. The onset was usually

heralded by a complaint of abdominal pain with fever, though rarely fever alone came first. The abdominal pain was general at times but frequently was limited to various regions of the abdomen. Pain in the right lower quadrant of the abdomen was not uncommon. When pain occurred over the kidneys it was severe and became excruciating if the region was palpated or the patient moved. There was no local edema or redness on these occasions. In some instances the hyperesthesia extended over the inner aspects of the thighs, but there was no erysipeloid reaction. Results of rectal examination were uniformly negative. Gaseous distention was common and frequently approached the severity of paralytic ileus. Abdominal rigidity was lacking unless there was peritoneal infection, but frequently voluntary rigidity was encountered. The rapid, grunting respirations accompanying severe

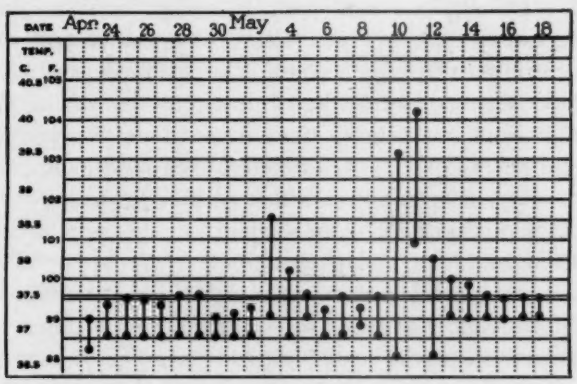

Chart 2.—Maximum and minimum daily temperatures of J. C., before, during and after two nephrotic crises with hypoaminoacidemia. Note especially the absence of fever preceding the attacks.

abodminal pain were not associated with any pulmonary involvement. The marked pallor of the child always became exaggerated, and the usual lively interest in the environment was replaced by prostration and listlessness. Cyanosis was observed only with concurrent infection. Nausea was common but vomiting less so; mild diarrhea was noted only occasionally. The most striking sign of an attack was that the child, usually lively, became suddenly prostrate, listless and pale. By chance, routine physical examination was made in 2 instances about forty-five minutes prior to an attack, and no abdominal tenderness was present, nor were there any other indications of the impending attack.

Recovery is as rapid as onset, and we have seen the temperature fall as much as 5 degrees (F.) in a few hours. A child who has been sick for many hours may suddenly sit up in bed and state that the pain

has gone and that he feels well again. Although secondary rises in temperature may occur for another twenty-four hours, the prostration is lacking.

During the attacks we continued to feed the children the same quantity of protein, carbohydrate and fat as previously. However, the diet was made liquid and fed on a four hour schedule. We have frequently given half the day's protein rations as gelatin, which has been well taken by the patients. Although it does not materially alter the course of the attack, we believe it to be of distinct value, for it furnishes an easily available source of amino acids, and we have the impression that with such a regimen the development of severe paralytic ileus is less common.

The clinical picture of acute illness accompanied a decrease in the plasma amino acids below 2.5 mg. of amino nitrogen per hundred cubic centimeters, as measured by the ninhydrin technic. The severity of the clinical manifestations was roughly proportional to the drop in plasma amino nitrogen below this value. We believe that the changes in the concentration of plasma amino acid occurred as abruptly as the changes in temperature and in the clinical condition of the patient, but it was not practicable to carry out more frequent bleedings on the patients because of the severity of the disturbance. The level of the amino acids in the blood was not apparently influenced by diet during the period of acute deficit in amino acid. One patient, R. F., was given a transfusion of 500 cc. of blood during an attack, with no appreciable improvement either in the plasma amino acid content or in the clinical condition.

In nephrotic children, ordinary infections in the upper respiratory tract, such as the common cold, otitis media, pharyngitis or cervical adenitis with high fever, are not accompanied by this acute metabolic disturbance. It was not cyclic in occurrence and bore no evident relation to any environmental factors.

The acute and characteristic changes noted in the plasma were not accompanied by constant findings in the blood cells. Determination of the cell amino nitrogen content by the technic used included both a red and a white cell count. Leukocytosis was always present during an attack, the white cell counts averaging 18,000 to 20,000. On one occasion (J. C., 3/25) the amount of cell amino acid increased strikingly; usually there was no significant change. The presence of glutathione in the cells, which reacts as an amino acid to both methods, rendered difficult any exact interpretation of the cell values. In addition, because of the difficulty of preparing cell solutions and of the necessity of carrying out their analyses immediately (the necessity does not exist with plasma), we discontinued routine determinations of the cell amino nitrogen content.

A characteristic finding during the attacks was that the nitrous acid method showed an increase in the amino nitrogen twelve to twenty-

four hours before the ninhydrin method. The clinical course paralleled the values obtained with the ninhydrin method. The significance of this variation is not known. The nitrous acid method determines all primary amino nitrogen in the blood, including that of any primary amines, amino purines and peptides that may be present but does not determine proline and oxyproline. The ninhydrin method includes both these amino acids, but excludes other amines and all peptides except those which, like glutathione, have an adjacent NH_2 and COOH group free in a glutamyl or aspartyl group. The specificity of the ninhydrin carboxyl method for the determination of amino acids has been discussed in detail by Van Slyke, Dillon and MacFadyen [11] and by MacFadyen and Van Slyke;[4] it appears to indicate closely the amino acid nitrogen content in analyses of plasma. The importance of using the ninhydrin method was demonstrated in the findings for G. B., who clinically had a characteristic attack in which the amount of plasma nitrogen as determined by the nitrous acid method was well above the critical level, while the ninhydrin method revealed the expected acute deficit.

The sharp decrease in plasma amino nitrogen occurred without significant change in the plasma nonprotein nitrogen or in the urea nitrogen. The changes observed in the plasma albumin and in the hemoglobin were slower in developing and did not parallel the clinical course of the acute illness to the same degree as did the changes in amino acid.

In addition to the sharp decline in amount of plasma amino acids during acute nephrotic crises, there may be a chronic deficit in plasma amino acids throughout the duration of the disease. From this chronic deficit in plasma amino acids there was a definite rise in the plasma amino nitrogen of J. T. during the period of observation; this rise paralleled clinical recovery and improvement in the plasma protein level. With recovery from the nephrotic syndrome the plasma amino nitrogen, as measured by the ninhydrin method, exceeded 4 mg. per hundred cubic centimeters. Unpublished data indicate that this may be the lower limit of normal. J. C. had a continuous amino nitrogen deficit during the entire period of study. The sharp increase in the plasma amino nitrogen of G. B., on the other hand, was not due to permanent recovery but was associated with rapid improvement immediately after her admission to the hospital. Subsequently her plasma amino acid nitrogen values again decreased to chronic deficit levels.

The decrease in plasma amino nitrogen during these crises was not due to failure to digest and absorb dietary protein, since the amount of urinary nitrogen excreted during these periods did not decrease nor was there any sigificant increase in nitrogen in the stool.[1c]

11. Van Slyke, D. D.; Dillon, R., and MacFadyen, D. A.: Gasometric Determination of Carboxyl Groups in Amino Acids, to be published.

The 2 patients fed a protein meal showed during the three hours after the meal a significant rise in the plasma amino nitrogen value as measured by both methods used. The results are given in table 2. Data on normal children for comparison are not available, but Peters and Van Slyke [12] summarized observations on adults in the conclusion that "In man . . . the maximum rise [in blood amino nitrogen after protein food] appears to be about 2 mg." per hundred cubic centimeters of whole blood. The data in chart 2, obtained by both the nitrous acid and the ninhydrin method, indicate increases of blood amino nitrogen of similar magnitude. Furthermore, an increase of 1 mg. or more in

TABLE 2.—*Data on Blood Amino Nitrogen, Hemoglobin, Plasma Proteins and Urea After Ingestion of a Protein Meal*

Patient	Period	Plasma Amino Nitrogen (Nitrous Acid Method) Mg. per 100 Cc.	Cell Amino Nitrogen (Nitrous Acid Method) Mg. per 100 Cc.	Whole Blood* Amino Nitrogen (Nitrous Acid Method) Mg. per 100 Cc.	Plasma Amino Nitrogen (Ninhydrin Method) Mg. per 100 Cc.	Cell † Amino Nitrogen (Ninhydrin Method) Mg. per 100 Cc.	Whole Blood Amino Nitrogen (Ninhydrin Method) Mg. per 100 Cc.	Plasma Ratio Amino Nitrogen (Nitrous Acid Method) to Amino Nitrogen (Ninhydrin Method)	Oxygen Capacity, Vol. per Cent	Total Plasma Protein, Gm. per 100 Cc.	Plasma Urea Nitrogen, Mg. per 100 Cc.
J. O.	Fasting.....	3.69	10.78	6.63	3.08	6.20	4.39	1.20	19.0	4.58	8.6
	45 min.....	4.68	10.57	7.18	4.15	6.80	5.30	1.13	19.3	4.31	9.9
	90 min.....	4.86	11.39	7.83	4.69	5.40	5.14	1.04	20.0	4.40	11.8
	135 min.....	5.39	11.66	8.05	4.69	6.80	5.62	1.15	19.2	4.29	11.1
	180 min.....	5.30	11.60	8.18	5.14	7.39	6.24	1.03	19.8	4.38	12.7
J. T.	Fasting.....	3.39	11.10	6.31	3.48	6.16	4.36	0.97	17.9	5.73	8.7
	45 min.....	5.06	12.62	7.63	5.24	6.96	5.67	0.97	16.9	5.33	12.1
	90 min.....	4.38	10.00	6.41	5.66	6.10	5.71	0.77	17.6	5.31	14.7
	135 min.....	4.51	11.98	7.18	5.60	5.07	5.26	0.81	17.4	5.67	13.0
	180 min.....	4.83	10.73	7.06	7.10	6.29	6.70	0.68	18.0	5.72	14.8

* By addition.
† Analyses done on tungstic acid filtrate.

the plasma amino nitrogen occurred in the first forty-five minutes after the meal. Evidently digestion, as well as absorption of the amino acids produced, began without delay.

A further point of general interest is the determination of the amino acid nitrogen content of the cells after the protein meal did not show changes which paralleled the changes in the plasma. The variations in cell amino acid content, ranging in the three hours over ± 5 per cent of the median value in each case, showed no regular relation to the process of protein digestion. The normally constant values obtained for hemoglobin, plasma albumin and total protein indicate that no serious disturbance of blood volume followed the withdrawal of samples for analysis.

12. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, vol. 1, p. 389.

An interesting difference between the data for the 2 patients who had eaten a protein meal was noted in the ratio of amino nitrogen determined by the nitrous acid method to amino nitrogen determined by the carboxyl method. For J. C. this ratio was never less than 1 and ranged from 1.20 during fasting to 1.03 three hours after eating. For J. T., on the other hand, the ratio never exceeded 1 and ranged from 0.97 during fasting to 0.68 after three hours. At present we have no information on the significance of these ratios.

COMMENT

Previous studies by other workers [13] of blood amino acids in nephritic and nephrotic patients have not revealed either the acute or the chronic type of disturbance. Many of the observations were made with the Folin colorimetric method which Van Slyke and Kirk [14] showed to be unreliable. In addition, most of the analyses were done on whole blood, in which the change would be difficult to detect because the amino nitrogen content of the cells is much greater than that of the plasma. Kirk [13] has reported from the clinic of the Rockefeller Institute work on amino nitrogen of plasma and of whole blood of nephritic and nephrotic patients. He used the Van Slyke gasometric nitrous acid method. Kirk confirmed the reports of previous workers that an increase in primary amino nitrogen may occur in adult nephritic patients, particularly those with severe renal failure. Kirk's youngest patient was 15 years old and had renal failure at the time of the study. It seems most likely that the contrast between the results obtained in studies of nephritis by previous workers and those in our studies is due chiefly to a difference in the type of patient studied. We have also carried out a few analyses on adults having nephrosis and to date have been able to substantiate Kirk's findings in cases of moderate to severe impairment of renal function. In an adult with nephrosis and a nearly normal urea clearance, we noted the same type of chronic deficit in plasma amino acid which has been here described as occurring in children. The acute disturbance of plasma amino nitrogen has thus far in our experience been limited to young children with the nephrotic syndrome.

SUMMARY

Two hitherto unknown disturbances of the amino acids in children with the nephrotic type of Bright's disease are described.

13. Cited by Kirk, E.: Amino Nitrogen Changes of the Blood in Nephritis, J. Clin. Investigation **12**:1091 (Nov.) 1933.

14. Van Slyke, D. D., and Kirk, E.: Comparison of Gasometric, Colorimetric and Titrimetric Determinations of Amino Nitrogen in Blood and Urine, J. Biol. Chem. **102**:651 (Oct.) 1933.

A chronic deficit in plasma amino acids often accompanies the disease. The content of plasma amino acid nitrogen is between 3 and 4 mg. per hundred cubic centimeters, in comparison with the usual normal content of 5 mg. or over. Recovery is accompanied by a rise in the plasma amino nitrogen to normal values.

An acute decline in plasma amino acid nitrogen to below 2.5 mg. per hundred cubic centimeters and sometimes to nearly 1 mg. per hundred cubic centimeters occurs uniformly with the clinical nephrotic crises described. The crisis occurs without infection. The acute clinical manifestations become apparent when the amino acid nitrogen drops below the critical level of 2.5 mg. per hundred cubic centimeters of plasma. Recovery from acute symptoms and return of plasma amino acid nitrogen to its previous level occur together. Recovery may be as rapid as the onset and take but a few hours.

The postprandial increase in plasma amino acid nitrogen after a heavy protein meal in the cases of 2 children with the nephrotic syndrome indicates no delay in protein digestion or absorption.

GIARDIASIS

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As has been shown by investigations and stated in a previous paper,[1] infection with the flagellate Giardia lamblia often causes complaints and symptoms. The three characteristic signs are: (1) abdominal complaints, (2) anemia and (3) retarded development.

The abdominal complaints may easily be explained by the mechanical action of the parasites. When the disease is severe the intestines are inundated by innumerable protozoa, several of them being attached to each epithelial cell by aid of their peristomes. (In rabbits Jassinowski [2] found a million organisms per square centimeter.) The flagellae protrude into the intestinal lumen and by their constant movement maintain a permanent inflammation.

The cause of the anemia has been studied for a long time. The supposition of Infurna [3] that the protozoon "eats red blood corpuscles" is not plausible, especially in view of the fact that no blood corpuscles or their fragments or any products of their metabolism could ever be demonstrated in the body of Giardia. The location of the parasite offers a more probable theory for the origin of the anemia. The primary and favorite habitat of the organism is the duodenum and the upper part of the ileum. According to many investigations, among them the experiments of Verzár, these parts of the intestinal tract have a role of utmost importance in hemopoiesis. It is not known whether the harmful effect of the protozoa is directed against the hemopoietic substances themselves (as, for instance, the "antianemic factor") or whether it influences only the absorption process, damaging this to such a degree that as a consequence anemia develops. That absorption is not normal in Giardia-infected children has been mentioned by Behnke.[4] He found that such patients often excrete fermentation stools because of incomplete absorption of carbohydrates. Steatorrhea was seen by Miller [5] in several cases of

From the Pediatric Department of the Royal Hungarian Peter Pázmány University.

1. Véghelyi, P. V.: Giardiasis in Children, Am. J. Dis. Child. **56**:1231 (Dec.) 1938.
2. Jassinowski, M. A.: Arch. f. Schiffs- u. Tropen-Hyg. **31**:191, 1927.
3. Infurna: Arch. ital. di sc. med. colon. **7**:185, 1926.
4. Behnke, H.: Ergebn. d. inn. Med. u. Kinderh. **39**:175, 1931.
5. Miller, R.: Arch. Dis. Childhood **1**:93, 1926.

giardiasis, and Manson-Bahr [6] stated that dejecta in this disease resemble the stools of sprue.

There is no satisfactory explanation for the retardation of development. It is true that the parasites withdraw a relatively large amount of nutritive material from the intestinal wall, but in view of the size of Giardia, the losses thus caused could never interfere with development if digestion and absorption were undisturbed. That is why I started to examine absorption in Giardia-infected children.

Fat [7] metabolism, fermentative activity and excretion of pigments were studied. The metabolism of proteins and carbohydrates could not be closely investigated, owing to the lack of time and the scarcity of means. But superficial determinations showed that the greatest disturbances are to be found in the absorption of fats; moreover, their variations are easier to evaluate than those of proteins or sugars.

Determination and estimation of ferments show whether the digestive processes, the conversion of nutritive substances into absorbable form, are unimpaired. Unless digestion is undisturbed, no conclusions as to the process of absorption can be drawn from the difference of ingested and excreted quantities. For instance, in cases of pancreatic insufficiency most of the fat taken in is again excreted, though the absorptive capacity of the organism is intact.

The excretion of urinary pigments may in certain cases characterize the absorption activity. A great part of the secreted bile is reabsorbed from the duodenum and the ileum (Croftan,[8] Tappeiner [9]) and is used again in bile formation. If, owing to some defect, the bile excreted into the intestines cannot be reabsorbed but is excreted with the feces, the organism suffers heavy losses; this explains the rapid loss of weight in animals with experimental fistulas of the bile duct. A part of the reabsorbed pigment is removed from the blood and excreted with the urine. If the amount of pigment absorbed by the intestine is less than normal, the pigment content of the feces will be increased while that of the urine is decreased.

SUBJECTS

The experiments were made on 17 children, who were selected from among 188 patients infected with Giardia, on the basis of the severity of their symptoms and the abnormality of their stools (steatorrhea, excessive fermentation and excessive acidity). Data in regard to them are summarized in table 1.

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6. Manson-Bahr, P.: The Dysenteric Disorders, London, Cassell & Co., Ltd., 1939, p. 266.

7. Fat means in this paper the total amount of substances extractible with purified petroleum benzine (petroleum ether) and alcohol.

8. Croftan, A. C.: Arch. f. Anat. u. Physiol. **90**:635, 1902.

9. Tappeiner, H.: Sitzungsb. d. k. Akad. d. Wissensch. **77**:281, 1878.

In table 1 the age is given in years and months, the hemoglobin value in percentage, the erythrocyte count in thousands and the retardation of development in months, on the basis of the tables of Schlesinger. Of the children studied 5 were boys and 12 girls. As can be seen in table 1 the average age was 8 years and 4 months; the average hemoglobin value, 63 per cent; the average erythrocyte count, 3,147,000 per cubic millimeter of blood, and the average retardation of weight, 29.3 months.

I wish to emphasize that apart from the infection with Giardia lamblia no pathologic condition was found in these children which could be held responsible for the symptoms. None was infected with syphilis or tuberculosis (all showed a negative reaction on intradermal injection of

TABLE 1.—*Data in Regard to Cases of Giardiasis Studied*

Case	Sex	Age Yr.	Age Mo.	Hemoglobin, %	Erythrocytes Count, in Thousands	Weight, Kg.	Retardation of Weight, Mo.	Determinations: Stool Fat	Urinary Pigment	Stool Lipase	Treatment
1	♂	1	7	70	4,100	7.80	11	+	+	..	..
2*	♂	2	1	62	3,220	6.85	17	+	+	+	+
3	♀	2	6	62	3,160	9.00	18	+	..	+	..
4	♀	6	1	60	3,000	16.50	19	+	+	+	..
5	♀	6	11	65	3,080	13.10	49	+	+	+	+
6	♀	7	..	40	1,780	19.50	9	..	+	..	+
7	♀	7	..	71	3,600	19.50	9	+	..	+	..
8	♀	8	..	44	2,080	22.50	3	..	+	..	..
9	♀	8	2	71	3,342	19.10	26	+	+	+	..
10	♂	9	..	68	3,240	22.20	23	+	..	+	..
11	♂	10	2	65	3,200	20.00	51	+	+	+	+
12	♀	10	3	70	3,300	23.70	24	+	+	..	..
13	♂	10	7	73	3,900	21.50	45	+	..	+	+
14	♀	12	..	62	2,710	26.00	35	..	+	..	..
15	♀	12	6	70	3,610	24.10	49	+	+	±	+
16	♀	13	6	62	3,000	23.90	62	+	+	+	+
17	♀	14	..	62	3,180	28.40	48	+	+	+	+
Average.....		8	4	63	3,147		29.3				
Controls....		7	6	86	4,280		+ 4.0				

* This case has been reported in detail in another paper (Véghelyi, P. V.: Celiac Disease Imitated by Giardiasis, Am. J. Dis. Child. **57**: 894 [April] 1939).

old tuberculin in dilutions ranging from 1:10,000 to 1:100), nor did many detailed tests (roentgen examinations, tests for gastric, liver and renal function and other tests) reveal the presence of other disease.

METHODS

The lipolytic activity of the feces was determined by the stalagmometric method of Rona and Michaelis.[10] Estimations were made according to the original directions, tributyrin and third-molar phosphate buffer solutions being used.

Determination of the total fat and its fractions was made by the method of Müller.[11] The more accurate method of Kumagawa and Suto could not be used, as it does not permit one to estimate the distribution of fat fractions (neutral fat, saponified and free fatty acids).

10. Rona, P., and Michaelis, L.: Biochem. Ztschr. **31**:345, 1911.

11. Müller, F.: Ztschr. f. klin. Med. **12**:51, 1887.

Determinations were made as follows: A weighed, aliquot part of the feces was dried at 100 C., weighed again, mixed with fat-free quartz sand and extracted with purified petroleum benzine U. S. P. (petroleum ether). After evaporation of the petroleum benzine the residue was weighed. An aliquot part of the remainder was dissolved in a mixture of alcohol and purified petroleum benzine and then titrated with alcoholic potassium hydroxide, phenolphthalein being used as an indicator. The result, multiplied by 0.0284, gives the quantity of free fatty acids expressed as stearic acid. This value subtracted from the whole extract gives the quantity of neutral fat. In order to determine the amount of saponified fatty acids, the extract of the feces was boiled with alcoholic hydrochloric acid, then dried, extracted with purified petroleum benzine and titrated with alcoholic potassium hydroxide. The fat content of the food was determined by simple Soxhlet extraction, purified petroleum benzine being used.

The metabolism was studied for periods of two to four days; these periods were preceded by a period of two to four days during which the patients were on an identical diet. In 4 cases (9, 12, 13 and 17) in which the experiments had to be brought to an end within four days, the metabolism was studied for only forty-eight hours, and the stools were marked at the beginning and end of the period by means of carmine. In the other cases the period of study lasted four days. The data given under "Experiments" are twenty-four hour averages of the resulting figures. The determination of fat in the diet was made from an aliquot portion of the entire food intake.

The concentration of urinary pigments was estimated according to the method of Veil[12] and Heilmeyer.[13] Freshly excreted urine was filtered (S. & S. no. 575 stiffened analytic filters were used), the specific gravity measured and the extinction determined with an L II green filter in a Zeiss stepphotometer, against water, 20 mm. cuvettes being used. If S is the specific gravity and D the value read, the quantity of urinary pigment is $F = \frac{20}{3} \log \frac{100}{D\%}$, and the concentration of pigment reduced to a specific gravity of 1.020 is $F_o = F \frac{20}{s} = \frac{400}{s} \log \frac{100}{D\%}$. The amount of pigment excreted in a day is $F.M = F \frac{\text{cubic centimeters of urine in 24 hours}}{100}$.

EXPERIMENTS

Lipase.—Determinations were made for 12 children (cases 2, 3, 4, 5, 7, 9, 10, 11, 13, 15, 16, and 17), comprising all but 2 of the children whose fat metabolism was studied. The value of the lipolytic activity of the feces was above 90 per cent for 7 children (cases 4, 7, 9, 10, 11, 13 and 17), between 80 and 90 per cent for 2 children (cases 2 and 3) and below 80 per cent for 3 children (cases 5, 15 and 16). The lowest value recorded, 76 per cent (case 5), is still above the pathologic level. Thus deficient or even decreased fermentative activity could not be detected in any of the children studied. It follows that the splitting of fat must have been normal in these children.

12. Veil, A.: Klin. Wchnschr. **2**:2217, 1927.

13. Heilmeyer, K.: Ztschr. f. exper. Med. **58**:532, 1927; **59**:283 and 573, 1928; **60**:626, 1928.

Fat Metabolism.—Studies of the fat metabolism were made for 14 children (cases 1, 2, 3, 4, 5, 7, 9, 10, 11, 12, 13, 15, 16 and 17). The results are shown in table 2.

Healthy subjects excrete no more than 1 to 6 per cent of the fat taken in with the food, as has been repeatedly shown. Even if one takes 10 per cent as the upper limit of normal, the values of only 4 children (cases 3, 7, 9 and 12) were within this figure. In 2 cases (the second determination in cases 2 and 16) less than 20 per cent of the ingested fat was absorbed, and in 6 cases less than half of it. The fat content of the

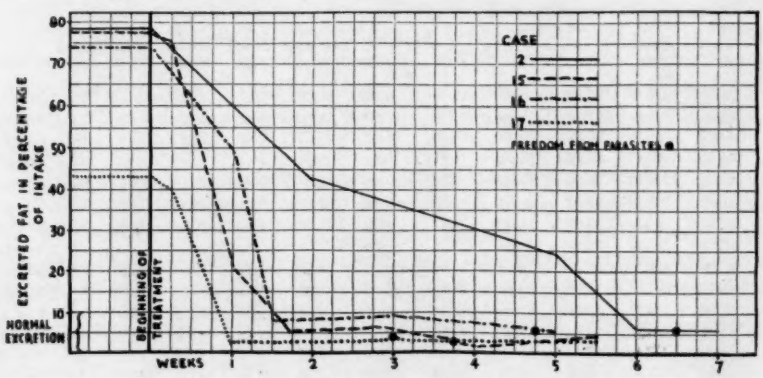
TABLE 2.—*Analysis of the Intake and Excretion of Fat in Fourteen Cases of Giardiasis*

Case	Intake of Fat, Gm.	Weight of Feces, Gm.	Dry Substance of Feces		Total Fat in Feces			Neutral Fat	Free Fatty Acids,	Saponified Fatty Acids,		Diet
			Gm.	%	Gm.	% of Intake	% of Dry Substance	% of Total Fat	% of Total Fat	% of Total Fat	pH of Feces	
1	24.20	410.0	36.50	8.90	17.10	70.80	46.80	35.7	53.2	11.1	5.6	Normal
2	42.30	290.0	57.40	19.80	32.90	77.90	58.00	30.1	62.6	7.3	3.8	Normal
	9.07	280.0	26.30	10.10	7.30	80.50	20.10	28.0	66.6	5.4	4.0	Fat-free
3	38.30	160.0	25.98	16.20	1.45	3.80	5.60	....	....	....	6.8	Normal
4	42.00	220.0	43.95	20.00	12.35	29.40	28.10	26.0	28.0	46.0	6.0	Normal
5	31.40	270.0	56.61	21.00	18.68	59.50	33.00	24.4	43.3	32.3	5.3	Normal
7	23.40	65.0	9.09	14.00	1.11	4.75	12.20	40.0	20.0	40.0	7.7	Normal
9	52.00	225.0	22.50	10.00	1.35	2.60	6.00	....	....	....	7.0	Normal
10	45.00	400.0	35.20	8.80	11.70	26.00	33.30	11.2	62.5	26.3	3.9	Normal
11	37.70	307.0	70.00	22.80	15.10	40.00	21.60	19.4	50.0	30.6	6.4	Normal
12	78.50	194.3	40.80	21.00	5.10	6.50	12.50	29.1	20.0	50.9	6.2	Normal
13	61.30	141.5	26.04	18.40	11.71	19.10	45.00	34.3	47.6	18.1	5.2	Normal
	12.55	182.0	22.31	16.90	2.76	22.00	12.37	....	....	....	...	Fat-free
15	39.65	517.7	73.00	14.10	30.69	77.40	42.00	27.9	48.9	23.2	4.0	Normal
	8.16	314.8	36.20	11.50	6.43	78.80	17.76	28.1	62.2	9.7	3.9	Fat-free
16	55.00	512.4	67.64	13.20	40.92	73.60	60.50	7.0	71.0	22.0	3.8	Normal
	8.70	450.0	33.00	7.33	7.54	86.70	22.80	10.6	66.6	22.8	4.0	Fat-free
17	157.00	405.0	97.00	19.00	67.82	43.20	70.00	20.6	29.6	49.8	5.8	Normal
	14.00	325.0	56.23	17.30	7.07	50.50	12.58	28.2	42.8	29.0	5.1	Fat-free

dry substance of the feces of normal persons is usually below 12 to 15 per cent. That of several of the children among the group studied was 50 per cent or more. The impaired absorption was not due to a fat intake which exceeded the tolerance of the children. Five of the subjects (cases 2, 13, 15, 16 and 17) were given a diet poor in fat and the fat metabolism studied again. The food remained the same as before with the exception that the fat was reduced to from a third to a tenth of the original amount. The results proved that the subjects were incapable of utilizing more of the fat even after the reduction. The percentage absorption remained roughly the same, the only changes being that after the fat content of the dry substance was decreased, the stools became less steatorrheic, their color, which had hitherto been grayish, became normal and the smell was less offensive. Accurate examinations, however, could easily

demonstrate that the reduction of fats had no effect on the pathologic condition itself; aside from the constantly deficient absorption capacity, no change could be demonstrated in either the composition of the fat or the excessive acidity of the stools.

The normal acidity of the feces varies, according to Freudenberg, between p_H 5.0 and 8.0. The stools of the Giardia-infected children were found to be usually more acid than this. This is due to the large amount of free fatty acid. Whereas normally only about one-fifth of the excreted fat appears in the form of free acid (the average given by Holt, Courtney and Fales[14] is 16.5 per cent), many times this quantity was found in the feces of nearly every patient. Free fatty acids comprised two thirds of the excreted fat in more than one instance, and the acidity of the feces reached such an extreme value as p_H 4.0 (table 2, last four columns).



Excretion of fat by 4 children with giardiasis before, during and after treatment.

Urinary Pigments.—Estimations of urinary pigment were made for 13 children (cases 1, 2, 4, 5, 6, 8, 9, 11, 12, 14, 15, 16, 17). The results are shown in table 3.

The concentration of pigment in the urine (F_0) is usually about 1.70. In that of healthy children, as is shown by the controls, it generally varies from 1.20 to 1.90. F_0 values of 0.50 are not pathologic for adults, but for normal children concentrations below 1.0 are extremely rare. The normal amount of pigment excreted during twenty-four hours (F. M) is about 10 to 14 cc. for men and 8 to 11 for women, while for children it has been found somewhat lower, mostly between 8 and 10 cc.

As for the data given in table 3, the high values in cases 4 and 12 must have been due to latent hepatic dysfunction not demonstrable by

14. Holt, L. E.; Courtney, A. M., and Fales, H. L.: Fat Metabolism of Infants and Young Children: IV. The Digestion of Some Vegetable Fats by Children on a Mixed Diet, Am. J. Dis. Child. **18**:157 (Sept.) 1919.

other methods. Normal values were obtained in cases 9 and 14. The values in case 8 can also be regarded as more or less normal, though neither the concentration of pigment in the urine (F_0) nor the amount of pigment excreted in a day (F. M) reached an average value. In the remaining 8 cases values were far below normal; several of the children did not excrete more than a tenth of the usual quantity. In the urine of 2 children (cases 2 and 15) the value for F_0 was below 0.10 and that for F. M below 1.0, while 4 children (cases 1, 5, 6 and 16) had values for F_0 between 0.10 and 0.20 and for F. M between 1.20 and 2.10, respectively.

Comment.—To sum up the results of the experiments, the feces of the patients contained an excessive amount of fat; some of them excreted

TABLE 3.—*Excretion of Urinary Pigments in Thirteen Cases of Giardiasis*

Case	Fo*	R.M*
1	0.12	1.91
2	0.095	0.99
4	4.10	19.46
5	0.13	2.05
6	0.11	1.22
8	0.88	6.70
9	1.72	8.33
11	0.30	2.00
12	5.00	25.00
14	1.60	7.80
15	0.09	0.82
16	0.17	1.52
17	0.46	3.11
Average of controls	1.78	9.79
Minimum of controls	1.07	7.70

* For explanation of terms "Fo" and "F.M," see text under "Methods."

most of the fat ingested; their stools were extremely acid, and the concentration of urinary pigments was far below normal.

COMMENT

The most frequent cause of steatorrhea is a complete or partial lack of ferments, due either to some dysfunction of the pancreas or to another condition. With such lack of ferments, the ingested fat, not being split, cannot be absorbed and is excreted with the stools. In the present cases this cause was excluded by the fact that the lipolytic activity of the feces of all the patients was normal and that the fat of the feces was split, that is, in a digested state. There are four more conditions that might have caused steatorrhea: celiac disease, acceleration of peristalsis, lack of adrenal cortex hormone and, finally, some mechanical obstacle. (No cases of sprue have ever been found in Hungary.)

Celiac disease can be excluded, as, with the exception of the patient in the second case, no children showed those symptoms that are essential characteristics of the celiac syndrome.

A primary acceleration of peristalsis, which was said by Freise and Jahr [15] to be the cause of deficient capacity for absorption in celiac disease, was not present in the patients in question. Roentgenographic examinations of the stomach and the intestines were made for 8 of the 10 children with steatorrhea, but no acceleration of peristalsis could be demonstrated. The frequency of bowel movements and the large quantity of stool passed by the patients are rather a consequence of the excessive acidity of the intestinal contents and of the fact that, in addition to poor absorption of fat, the absorption of other nutritive material, such as water and secretions, is impaired.

According to the experiments of Verzár [16] and Laszt,[17] after extirpation of the adrenal glands fats cannot be absorbed, and marked difficulty is noted in the metabolism of salts and carbohydrates as well. The cause of this difficulty is the lack of the adrenal cortex hormone, the regulator of fat synthesis in the villi. If the hormone is not present, only fatty acids can be found in the intestinal mucous membrane, no neutral fat. In the literature at my disposal I could not find any certain case of idiopathic steatorrhea of this origin. In such a case, of course, there should be, in addition to defective absorption, other symptoms of addisonism. As similar signs were not presented by the patients in the present series, this cause may be excluded, too.

The last possibility was that absorption was mechanically impaired by some cause, rendering the wall of the intestines impermeable. This assumption was also supported by the decrease of urinary pigments.

The concentration of pigment in the urine (F_0) depends on the quantity of salts and pigment. The concentration is low if less pigment is excreted or if the amount of dissolved substances responsible for raising the specific gravity (salts, urea and sugar) increases. The concentration is low after meals; F_0 may decrease to 0.40 in states of excitement (nervous polyuria, effect of caffeine, etc., when the excretion of salts is always increased) and in diabetes. No condition in which concentration decreases to such values as in the present cases or in which this phenomenon is caused by a real reduction of pigments instead of an increase of dissolved substances has hitherto been described. Neither is there any condition known in which the intestinal wall becomes impermeable. Still, this is the only possible explanation of the fact that the easily absorbable bile constituents fail to get into the blood from the intestine. (There was no reason for supposing that there were defects in the production or secretion of bile.) This situation can be explained only on the basis of mechanical interference.

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15. Freise, K., and Jahr, J. M.: Jahrb. f. Kinderh. **110**:205, 1925.
16. Verzár, F., and Laszt, A.: Biochem. Ztschr. **288**:351, 1936.
17. Laszt, A.: Biochem. Ztschr. **285**:356, 1936; **292**:159, 1937.

The physical obstacle forming the basis of both the defective absorption and the reduction of urinary pigments is probably a layer of parasites. On the basis of the aforementioned observation of Jassinowski, one may suppose that in grave infections protozoa may be present in such quantities that they cover almost every active area of the bowels, thus forming an impermeable obstacle between the intestinal lumen and the organism proper.

The correctness of this assumption, i. e., that the masses of Giardia adhering to the intestinal wall interfere with absorption activity, can be substantiated only through treating the patients. If the supposition is right, conditions will be restored to normal by expulsion of the parasites.

RESULTS OF TREATMENT

Treatment was started for 12 children of the 17, but systematic reexaminations of only 8 could be made.

Acetarsone and acridine compounds were used as drugs. No other medicaments were given to the children during the entire course of treatment, and no special diet was prescribed. All 8 were freed from the parasites, recovery taking from three and a half to seven weeks. Treatment was continued until cysts could no longer be detected in the stools after a provocative test with sodium sulfate on three consecutive days. In order to check conditions of absorption, the same studies were made after treatment as before. Generally, the reexamination took place two to four weeks after the stools were found to be normal, the period between the original and the final examination being from seven to twelve weeks. In 4 cases the course and progress of recovery were observed throughout. Details are compiled in table 4.

It can be seen from table 4 that normal conditions were found after treatment. Utilization of the fat became perfect, no more than one tenth to one twentieth of the consumed amount was excreted and the fat content of the feces decreased to the normal values of 7 to 10 per cent. The same was found with regard to the excretion of pigments. The concentration of pigment in the urine became normal, F_0 being about 1.0, except in 1 case (6), while the amount of pigment in the urine excreted in twenty-four hours increased, F. M being between 8 and 12.

Improvement was gradual but began soon, on about the fourth or fifth day after treatment had been started. In order to illustrate its progress, the values for the excretion of fat of 4 of the children (cases 2, 15, 16 and 17) observed throughout the experiment were compiled in a chart. The amount of fat excreted is calculated in percentage of total fat intake.

The chart shows that absorption became normal even before the complete disappearance of the protozoa. (Freedom from parasites is

shown by a circle on the curves.) The whole intestinal surface is not normally needed for absorption, and it is probable that the area set free by a reduction of the parasites is sufficient to meet the requirements of normal absorption. The behavior of the concentration of pigments in the urine was similar. Restoration to normal excretion always preceded that of the absorption of fats. It seems that a smaller intestinal surface is needed for absorption of pigments than of fats, owing either to their greater ease of absorption or to their smaller absolute quantity.

TABLE 4.—*Fat Absorption and Concentration of Urinary Pigment in Eight Children with Giardiasis Before and After Treatment*

		Total Fat in Feces		Urinary Pigment	
Case	Treatment	% of Intake	% of Dry Substance	Fo*	F.M*
2	Before	77.90	58.00	0.095	0.99
	After	5.60	7.70	1.79	8.00
5	Before	59.50	33.00	0.13	2.05
	After	9.30	10.40	1.10	9.90
6	Before	.....	.....	0.11	1.22
	After	.....	.....	0.90	5.62
11	Before	40.00	21.60	0.30	2.00
	After	10.10	8.00	1.43	9.70
13	Before	19.10	45.00	....	....
	After	4.70	6.90	....	....
15	Before	77.40	42.00	0.09	0.82
	After	5.20	12.10	1.98	8.75
16	Before	73.60	60.50	0.17	1.52
	After	7.10	9.30	1.44	9.32
17	Before	43.20	70.00	0.46	3.11
	After	3.30	10.00	1.66	12.40
Average	Before	55.81	47.16	0.22	1.67
	After	6.50	7.80	1.46	9.10

* For explanation of terms "Fo" and "F.M," see text under "Methods."

I could not find any parallelism between the number of excreted cysts and the severity or the amelioration of symptoms. Neither was it possible to find any relation between the degree of interference with absorption and the clinical state. This is natural if one considers that there are no means of establishing how long the infection has lasted and how long the organism has suffered from deficient absorption.

The various complaints and symptoms disappeared simultaneously with the progress of recovery. The number of discharges and the quantity of stools were reduced to normal. The preponderance of free fatty acids vanished, and thus the feces became less acid in reaction. In the second or third week after treatment was begun, stools were seldom found to be more acid than p_H 5.0. The complaints of the patients (abdominal pains, weakness, headache and dizziness) disappeared after

cure. Complete clinical recovery required a certain time after freedom from parasites was obtained, since the consequences of their long residence had to be overcome. It was striking how promptly anemia responded to treatment. Increase in weight of the greatly underdeveloped children (some were retarded four or five years according to the average for their age) started promptly, and the weight put on in two to four months corresponded to two or three years' development of a normal child of the same age. Data in regard to the 8 children in question are summarized in table 5.

TABLE 5.—*Hemoglobin Values, Erythrocyte Counts and Development in Eight Children with Giardiasis Before and After Treatment*

Case	Treatment	Hemoglobin Value, %	Erythrocyte Count, Thousands	Weight, Kg.	Gain in Weight Over Normal in Mo.	Period Between First and Last Examination, Mo.
2	Before	62	3,220	6.85		
	After	78	4,700	11.75	5	3
5	Before	65	3,080	13.10		
	After	99	5,320	16.90	17	5
6	Before	40	1,780	19.50		
	After	80	4,440	24.00	21	5
11	Before	65	3,200	20.00		
	After	86	4.480	22.30	11	4
13	Before	73	3,900	21.50		
	After	102	5,000	28.10	31	3
15	Before	70	3,610	24.10		
	After	81	4,480	28.80	18	2
16	Before	62	3,000	23.90		
	After	93	4,800	31.40	28	3
17	Before	62	3,180	28.40		
	After	100	5,050	36.20	21	2
Average	Before	62	3,121	.....		
	After	90	4,781	.....	19	2½

COMMENT

From the foregoing observations it may be taken as established that the symptoms of children infected with Giardia lamblia are due to disorders of absorption. The parasites almost cover the active surface of the intestine and interfere with absorption by forming an impermeable layer. The degree of impairment is probably proportional to the area of intestinal surface rendered inactive. If this surface is small, capacity for absorption may remain intact, and no symptoms will arise. This may be the explanation of the fact that "healthy carriers," i. e., infected persons who show no symptoms, are not a rarity. Common methods of examination do not reveal deficiencies unless infection has spread to considerable areas. Finally, infections may be severe enough to paralyze

extensive intestinal surfaces, thus leading to a condition similar to atrophy from inanition. This state is further aggravated by the fact that besides foodstuffs other important substances, such as bile and vitamins, are not absorbed either and also by the fact that a great part of the available supply of calcium and magnesium is expended in binding the excess of free fatty acid. In this respect the condition resembles celiac disease. The similarity of these two diseases has been pointed out by R. Miller [5] and was shown in my case 2.

Several authors still deny that Giardia lamblia may cause disease. The experiments described will, I believe, prove the pathogenicity of this organism. One of the main problems however, is, still unsolved: It is not known what the factors are that sometimes hinder the reproduction of these protozoa and at other times allow them to multiply and cause symptoms.

SUMMARY

Absorption of fat and excretion of pigment in the urine were examined in 17 children infected with Giardia who were selected from 188 patients. None of them showed evidence of disease other than the parasitic infection. Fat absorption was found to be greatly defective, and only a small part of the normal amount of urinary pigment was excreted. The condition was attributed to the mechanical effect of the parasites covering the wall of the intestines and rendering it impermeable. The resulting difficulty in absorption gave rise to symptoms common in giardiasis—anemia and retardation of development. All the symptoms disappeared after the expulsion of the parasites. The fat absorption and pigment content of the urine became normal, anemia improved and rapid growth commenced.

HANDS AND WRISTS OF THE DIABETIC CHILD

A ROENTGENOLOGIC STUDY

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This study was undertaken primarily to obtain data concerning the osseous ages of a group of diabetic children, to observe the variations from the chronologic ages and the incidence of anomalies and developmental defects.

Ninety-five boys and 74 girls are included, a total of 169 consecutive patients. The material included at first only retarded children and later all children who reported for physical examination. This gave a high incidence of retarded children, 30 per cent, as contrasted with an incidence of 10 per cent among 1,400 diabetic children. White [1] has classified as significantly retarded any patient who measures 4 inches (10 cm.) below Baldwin's and Wood's average height for age.

The hands and wrists were selected for study because more centers of ossification are present in this region than in any other, because a more thorough investigation has been made of this area and because excellent standards for comparison are available. Both hands were observed in all cases. The differences between them were usually in delayed appearance or delayed development of a center of ossification, usually of a carpal bone, in one hand accompanying the development of a normal center in the corresponding bone of the other hand. Less frequently developmental defects demonstrated by bony irregularities were observed in only one hand.

Before I began this study I compared roentgenograms of the hands taken with the standards of Flory.[2] When Todd's [3] monograph was published, I became interested in his method of assessment, that of accepting only the most advanced determinators of maturity and of disregarding the time of appearance of the centers of ossification. Todd

From the George F. Baker Clinic, New England Deaconess Hospital, Dr. Elliott P. Joslin, Medical Director.

1. White, P.: Diabetes in Childhood and Adolescence, Philadelphia, Lea & Febiger, 1932.

2. Flory, C. D.: Osseous Development in the Hand as an Index of Skeletal Development, Monograph of the Society for Research in Child Development, National Research Council, 1936, vol. 1, no. 3.

3. Todd, T. W.: Atlas of Skeletal Maturation (Hand), St. Louis, C. V. Mosby Company, 1937.

placed little reliance on the carpal bones, depending chiefly on the appearance of the metacarpal bones and the phalanges. His detailed description of the growing ends of the bones and of the centers of ossification and the fact that his standards are made at six month intervals are very helpful. I should assess the children by Vogt and Vickers'[4] standards if it were not for the fact that the ages of so few of the children in my series are in the period for which standards are available. These standards would be especially desirable for these children, since most of them came from the same geographic location.

In some of the roentgenograms used in this study certain determinators of maturity were comparable to one of Todd's age standards and certain other determinators to other age standards. When only the most advanced determinators (Todd's method) are accepted, the child is given an advanced rating. It is in such instances that there may occur considerable difference in the assessment of age according to whether Todd's or Flory's standards are used, Todd's assessment being in advance of Flory's. Another factor which gives the children a more advanced rating according to Todd's methods is the omission from consideration of the absence or the delayed appearance of centers of ossification.

The differences that may occur in assessment by Todd's or by Flory's method are illustrated by the case of G. M. (fig. 1), a well developed 4 year old boy. The hand shown in the roentgenogram was assessed by Todd and was considered by him to show maturity somewhat above his chronologic age. By Flory's standards there is definite retardation, only two carpal centers being present instead of four. According to Flory's standards the cuneiform bone should appear at 2 years of age and the semilunar bone at 4.

In spite of the considerable differences in individual cases, the ages as determined by Todd's and by Flory's standards are the same or vary up to 3 months, plus or minus, for 67.9 per cent of the boys and 68.8 per cent of the girls. The greatest variation in the ages of the boys is 21 months and in those of the girls 9 months.

I have accepted both Todd's and Flory's chronologic ages as applied to their standards. Todd said that his standards are successive standards of progressive maturity and do not of necessity represent any particular chronologic age. They do correspond to the chronologic ages of the Cleveland children examined. Only healthy children whose parents took enough interest in their welfare to have them periodically

4. Vogt, E. C., and Vickers, V. S.: Osseous Growth and Development, Radiology **31**:441 (Oct.) 1938.

examined by a physician were used in the production of Todd's standards. Thus children from all classes of society are included. Flory's material consisted of children attending the University of Chicago Laboratory School except in his older and younger age periods. The older and younger children were from all social strata. The younger

Fig. 1.—Hand of a 4 year old boy with diabetes of thirteen months' duration; osseous age 4 years and 9 months according to Todd's standards and 3 years according to Flory's standards. Note pseudoepiphysis of the second metacarpal bone.

came in part from the Chicago Lying-In Hospital and from among the children of parents in the university community. The older boys and girls were from the Chicago Junior College.

I hope to collect the growth curves of the hands of a large number of diabetic children. If roentgenograms were taken at sufficiently fre-

quent intervals, one might ascertain at just what time the process of maturation was retarded or arrested temporarily and correlate that observation with the clinical picture. Although at the present time I have the curves of very few children and in most cases for short periods of time, these curves proved helpful to me in estimating the results of therapy. The importance of roentgenologic examinations for this purpose has been emphasized by Shepardson.[5]

The hands illustrated in figure *2A* are of a boy 10 years and 6 months of age in whom diabetes developed at the age of 12 months. This roentgenogram was taken because of injury and not for this study. Centers of ossification of four carpal bones are present on the left and of three on the right. Two centers of ossification appear in each semilunar bone. Figure *2B* shows the hands of the same boy ten months later. It can be seen that there is a marked change in the contours of the metacarpal epiphyses and the proximal ends of the shafts and also in the epiphyses of the first row of phalanges. Centers of ossification have appeared in the trapeziums, the trapezoids, the right scaphoid and the ulnar epiphyses. All the bones are larger and contain more calcium. The first film suggests an age of 5 years and 3 months and the second an age of 7 years and 9 months, a growth of 30 months in a ten month period.

Since the variations between the ages as determined by Todd's and those as determined by Flory's standards were slight except in a few instances, only the former ages are here reported. Any variation in the osseous age from the chronologic is recorded. A record of this kind gives a better idea of the trend of development even though the particular child is considered normal. It seems to me that a variation of six months, plus or minus, should be considered normal. It is known that healthy children show at least that amount of variation.

If one accepts a variation of six months, plus or minus, one finds that in this series the osseous growth of 25.9 per cent of the boys and 33.2 per cent of the girls is normal; that of 60.2 per cent of the boys and 51.1 per cent of the girls is retarded; that of 13.8 per cent of the boys and 15.6 per cent of the girls is accelerated. That is, 9.1 per cent more boys than girls have retarded osseous growth, and 7.3 per cent fewer boys have normal osseous growth.

The osseous growth of 24 (14.2 per cent) boys and 11 (6.5 per cent) girls or a total of 35 children (20.7 per cent) is retarded more than two years, and that of 23 children (13.6 per cent), more than

5. Shepardson, H. C.: Osseous Development in Endocrine Diagnosis, Radiology **26**:685 (June) 1936.

three years. Seventeen of the latter are boys, and 6 are girls (figs. 3 and 4). Shelton [6] found an osseous retardation of two years or more in 15 per cent of 560 unselected children in Santa Barbara County (California) public schools. The percentage of roentgeno-

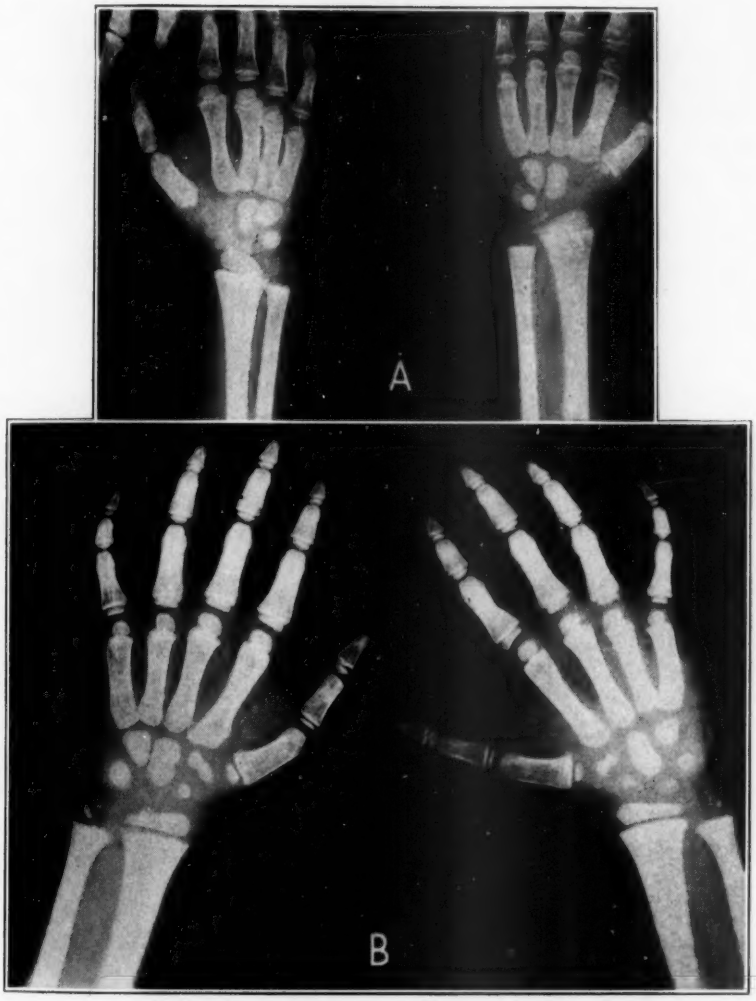

Fig. 2.—*A*, hands of a boy of 10 years and 6 months with diabetes of nine years and six months' duration and an osseous age of 5 years and 3 months. Note two centers of ossification of the semilunar bone; *B*, hands of the same boy ten months later; chronologic age 11 years and 4 months, osseous age 7 years and 9 months.

6. Shelton, E. K., cited by Clark, D. M.: The Practical Value of Radiography of the Epiphyses in the Diagnosis of Preadult Endocrine Disorders, Am. J. Roentgenol. **35**:752 (June) 1936.

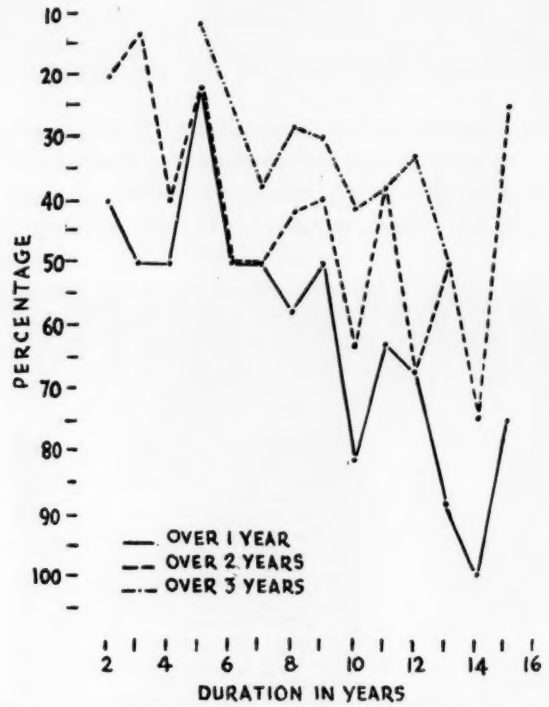

Fig. 3.—Percentage of diabetic boys with osseous retardation of more than twelve months.

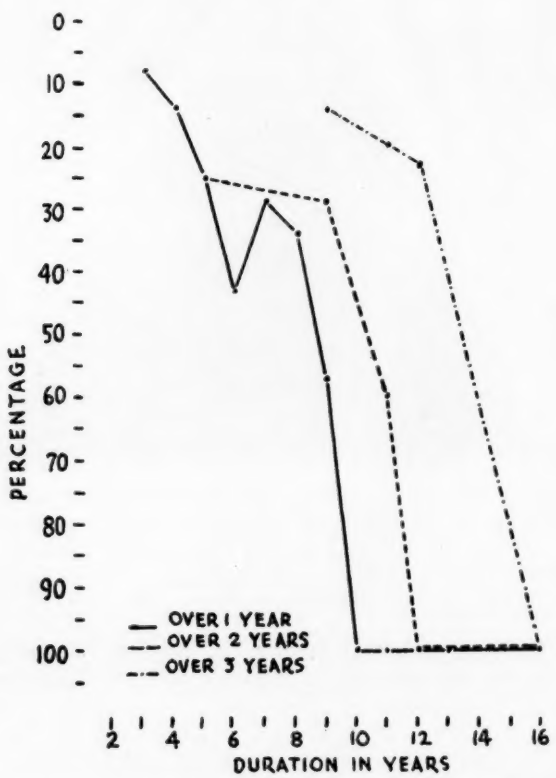

Fig. 4.—Percentage of diabetic girls with osseous retardation of more than twelve months.

logically studied diabetic children with osseous retardation of more than two years is only 5.7 per cent greater than that of his unselected children.

The greatest amount of retardation observed in a male was seven years. This amount occurred in a man of 26 years with diabetes of twelve years' duration. The greatest amount of retardation seen in a female was nine years. This amount occurred in a 25 year old woman with diabetes of eighteen years' duration.

An inconstant increase in the degree of retardation is noted with an increase in the duration of diabetes. There is also an inconstant increase in the degree of retardation with an increase in the age of the patient. In the cases studied, however, it is to be noted that the older the patient the longer the duration of diabetes, as a rule. Curves illustrating the retardation according to duration and to age are seen in figures 5 and 6, respectively.

Among children with diabetes of the same duration, the patients having osseous retardation, with few exceptions, were older (by from one month to eight years in boys and from three months to ten years in girls) than the patients with normal or accelerated growth. It is to be noted in figure 5, which shows the average amount of osseous retardation or acceleration of all boys in relation to the duration of diabetes, that after the first year there is osseous retardation in boys with diabetes of all durations. If, however, instead of taking the average osseous retardation of boys with diabetes of each duration one divides the patients into those with accelerated, with normal and with retarded development, it is found that development may be accelerated in boys who have had diabetes as long as thirteen years. Among girls the average for all members of each group shows retardation after the third year, but on dividing each group as was done with the boys one finds that development may be accelerated in girls who have had diabetes as long as nine years (fig. 7).

Pseudoepiphyses of the second metacarpal bones occurred in 14.7 per cent of boys and 5.3 per cent of girls. Flory [2] reported an incidence of 4.4 per cent and Carter [7] an incidence of 1 to 2 per cent in normal children. Stettner's [8] figures show an incidence of 16 per cent. This high incidence may be due to the fact that he included a number of patients with multiple congenital anomalies and defects. He reported the presence of pseudoepiphyses of metacarpal bones and phalanges in general in 23 per cent of boys and 21 per cent of girls without congenital defects or anomalies.

7. Carter, T. M., cited by Flory,[2] p. 23.

8. Stettner, E.: Ossificationsstudien am Handskelett: II. Ueber Pseudoepiphysen des Handskeletts, Ztschr. f. Kinderh. **51**:459, 1931.

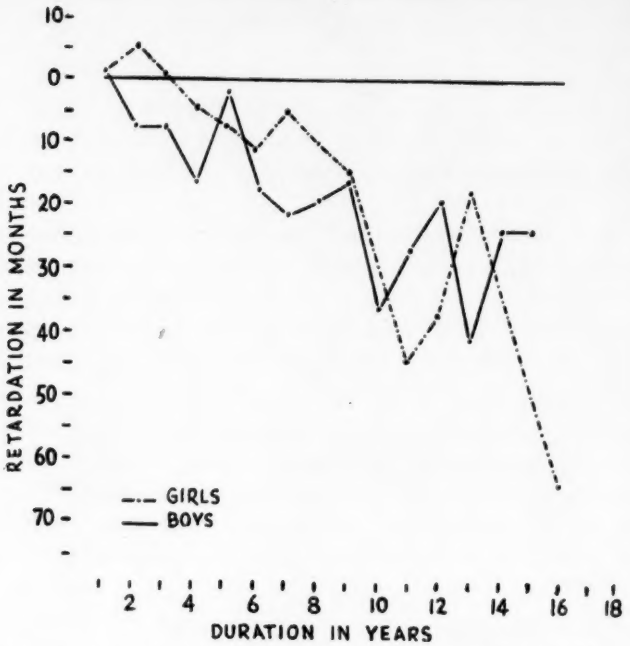

Fig. 5.—Development of the hands and wrists of children in relation to duration of diabetes.

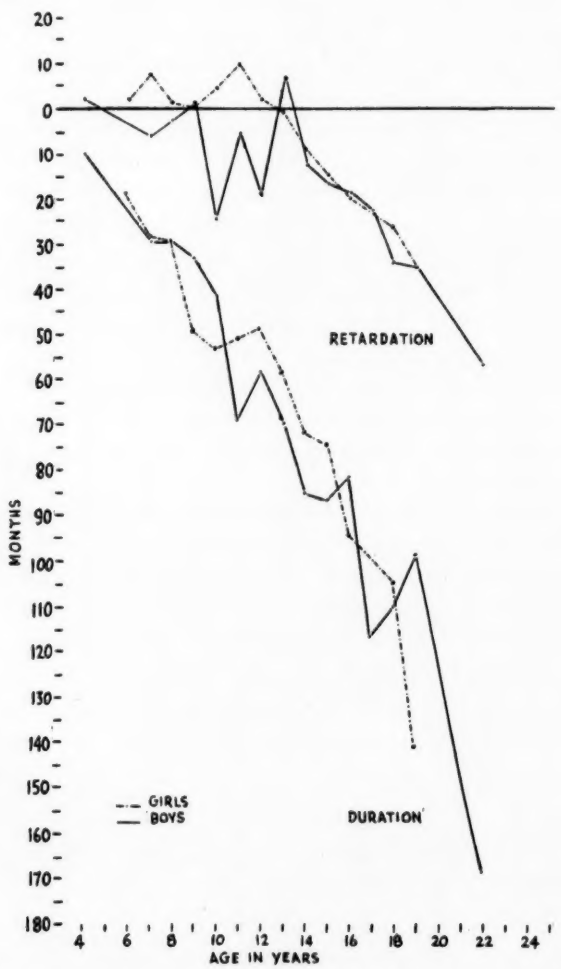

Fig. 6.—Development of the hands and wrists of diabetic children in relation to age.

Pseudoepiphyses of the phalanges, lateral or mesial flexion of the fingers, brachydactylism and fusion of the carpal bones were observed.

Delicate bridges of bone extending from the ulnar epiphyses to the shafts and occasionally upward as dense lines into the shafts were observed in several children. A single bridge may occur on one side only or on both sides; rarely two or three bridges are present on each side. The bridges are approximately a millimeter in diameter and appear to lie near the margins of the epiphyses rather than in the central por-

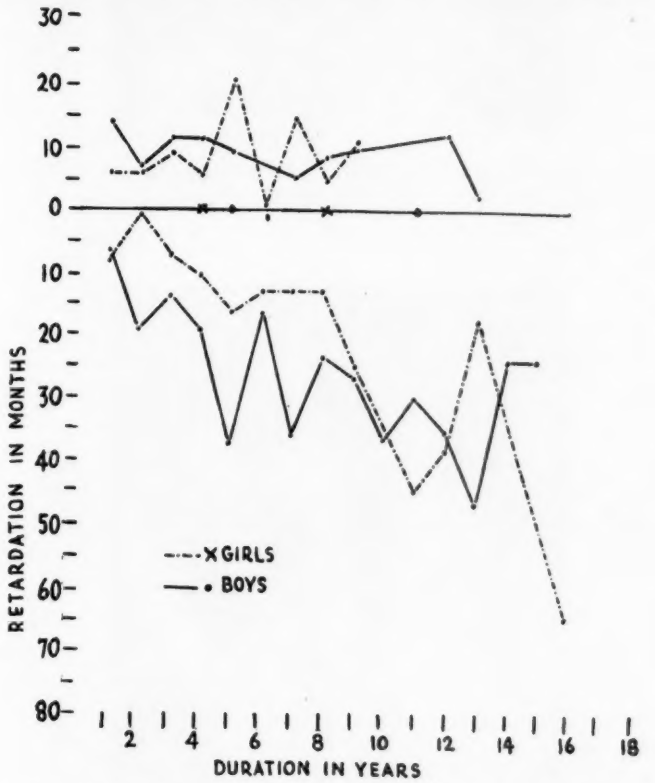

Fig. 7.—Development of the hands and wrists of children in relation to the duration of diabetes. Each group of patients is subdivided into those with accelerated, normal and retarded development.

tions. They may stop abruptly at the junction with the metaphyses or continue as dense lines into the shafts for a distance of 2 or 3 mm. up to 3 or 4 cm. Roentgenograms of the wrists of 13 boys, 13.7 per cent, and of 6 girls, 7.9 per cent, showed these bridges. Such bridges also appeared in the wrists of 2 nondiabetic children of whose wrists roentgenograms happened to be made during the time these diabetic children were studied. These bridges (figs. 8 and 9) have been observed in the

Fig. 8.—Roentgenogram of the wrist. Observe the delicate bridge of bone extending from the epiphysis to the metaphysis and upward for a short distance as a dense line.

Fig. 9.—Hand and wrist of a diabetic boy of 8, a hypothyroid dwarf. Two bridges of bone connect the ulnar epiphysis and metaphysis. Observe the thickened epiphysis of the first phalanx of the little finger.

wrists of boys from the age of 6 years and 7 months up to 14 years and 4 months and in those of girls from 9 years and 6 months up to 13 years and 11 months.

I have not been able to observe these children over a long enough period to see what change takes place in the bridges. The longest interval between roentgen examinations of any of these children was seven months, and in the films taken at that interval the appearance remained unchanged. The oldest boy, 14 years and 4 months, and the oldest girl, 13 years and 11 months, showed no evidence of a narrowing of the epiphysial line, suggesting premature closure.

One seventh of the children had anomalies with or without developmental defects. The incidence of boys with anomalies is 16.8 per cent and of the girls 10.8 per cent. The incidence of children with developmental defects is 15.9 per cent. Defects occurred twice as frequently in boys as in girls. The total incidence of children with anomalies and developmental defects is 24.3 per cent.

SUMMARY

Roentgenograms of the hands and wrists of 95 boys and of 74 girls have been assessed by Todd's and by Flory's standards to ascertain the osseous ages. Anomalies and development defects have been noted.

The osseous and chronologic ages are the same or vary up to 6 months, plus or minus, for 25.9 per cent of the boys and 33.2 per cent of the girls. The osseous ages are retarded for 60.2 per cent of the boys and 51.1 per cent of the girls, and are accelerated for 13.8 per cent of boys and 15.6 per cent of girls.

Twenty and seven-tenths per cent of the children have retardation of osseous growth of more than two years, and 13.6 per cent have retardation of more than three years. The incidence of boys showing retardation is greater than that of girls.

In the subjects studied, the longer the duration of diabetes the greater the tendency to retardation. Among persons with diabetes of the same duration the average age of the children with retardation was greater than of those with normal or accelerated osseous growth.

Anomalies and developmental defects were observed in one fourth of these diabetic children.

CONCLUSIONS

Anomalies and developmental defects occur more frequently in the diabetic than in the nondiabetic child.

The high incidence (20.7 per cent) of retardation of more than two years in these children and the retardation of all boys with diabetes of more than thirteen years' duration and of all girls with diabetes of more than nine years' duration, suggest that diabetes mellitus plays some part in the delayed development.

A STUDY OF TWO HUNDRED AND FORTY BREAST-FED AND ARTIFICIALLY FED INFANTS IN THE ST. LOUIS AREA

I. A COMPARISON OF PROPHYLACTIC ANTIRACHITIC EFFECTS OF 135 AND 200 UNIT IRRADIATED EVAPORATED MILKS, 200 UNIT IRRADIATED FRESH MILK AND HUMAN AND NONIRRADIATED EVAPORATED MILK FORTIFIED WITH 800 TO 1,000 UNITS OF VITAMIN D AS VIOSTEROL

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ST. LOUIS

A study to determine the effects of different types of vitamin D administration on young infants in St. Louis has been carried on for a period of twenty months, beginning in September 1937. The present report is confined to observations on the growth and development of the infants and on the incidence of rickets. Observations on the incidence of feeding difficulties, gastrointestinal disturbances and rashes will form the basis of a subsequent communication.

METHOD

Babies were selected from the wards of the St. Louis Maternity Hospital and the St. Louis City Hospital. They were normal, healthy infants weighing at least 5 pounds (2,268 Gm.) at birth, and the mothers were intelligent and willing to cooperate. Primiparas formed the largest part of the maternal group. Within a week after discharge from the hospital, each mother and child were visited by the trained nurse of the clinic. The nurse was capable and had had extensive experience in the care of infants. Her visit served several purposes: The mother received instruction, when necessary, in the details of caring for the baby and in the preparation of the formula; a report of home conditions and of the intelligence and cooperation of the family was returned to the clinic. Undesirable subjects were omitted from the investigation; additional ones were chosen to fill the quota.

Two hundred and eight infants were divided into eight groups with regard to their type of feeding and source of vitamin D (table 1). An effort was made to have at least 25 infants in each group. They were put on the formula of their respective group before the tenth day of life. Group 1 served as a control, consisting of breast-fed infants who received 5 drops of viosterol in oil (800-1,000 U. S. P. units of vitamin D) daily. Groups 2 and 3 (N. I. E. + V 5) were fed nonirradiated evaporated milk plus 5 drops of viosterol daily. Groups 4 and 5

From the Department of Pediatrics, Washington University School of Medicine and the St. Louis Children's Hospital, under a special grant from the Wisconsin Alumni Research Foundation.

(E-135) were fed irradiated evaporated milk assaying 135 U. S. P. units of vitamin D to the reconstructed quart. Groups 6 and 7 (E-200) received irradiated evaporated milk assaying 200 units. Group 8 (W. M.-200A) received irradiated whole milk assaying 200 units. The formulas of infants in groups 3, 5 and 7 were acidified with 0.5 per cent lactic acid.

Because, rather unexpectedly, at the end of nine months the incidence of rickets in the group receiving 200 unit irradiated whole milk was less than in that receiving 200 unit irradiated evaporated milk, a second group, born in a different quarter of the year, was started on whole milk feeding (W. M.-200 B); also a small group was started on 135 unit irradiated evaporated milk plus 15 drops of viosterol in oil (2,500-3,000 U. S. P. units of vitamin D) as a control (E-135 + V 15).

Each patient made his first visit to the clinic when between 5 and 6 weeks of age. At this time a careful history, including information as to familial disease, antepartum diet of the mother and feeding difficulties, was taken; roentgenograms of the right wrist were made; all infants were started on orange juice, 1 ounce (30 cc.) daily (later tomato juice was substituted in a few cases), and the infants in groups 1, 2 and 3 were started on 5 drops of viosterol in oil [1] (800-

TABLE 1.—*Grouping of the Observed Infants According to Type of Feeding and Source of Vitamin D*

Group	Feeding
1	Breast milk + viosterol in oil 5 drops (V5)
2	Nonirradiated evaporated milk + viosterol in oil 5 drops (N.I.E.+V5)
3	Nonirradiated evaporated milk + viosterol in oil + lactic acid (N.I.E.+V5)
4	135 unit evaporated milk (E-135)
5	135 unit evaporated milk + lactic acid (E-135)
6	200 unit evaporated milk (E-200)
7	200 unit evaporated milk + lactic acid (E-200)
8	200 unit fresh homogenized milk (W.M.-200A)

1,000 U. S. P. units of vitamin D) daily. Physical examination on this and subsequent visits was complete and included measurements of weight, height, head and chest. The patients were seen every four weeks. Roentgenograms were taken every eight weeks as a routine. If, however, the roentgenogram showed questionable or active rickets, roentgenograms were made every four weeks until the process was healing.

A chart was kept by each mother for a daily record of feeding, vomiting, stools, irritability and other pertinent matters. If the infant became ill the mother communicated with the clinic and received advice or brought her baby in for treatment. Further visits were made by the nurse when indicated.

Equivalent formulas were used for the various groups and blue label Karo corn syrup was the carbohydrate addition in all. Cereal, usually pablum [2] or oatmeal, was added when the child weighed 12 to 13 pounds (5.5 to 6 Kg.) and then vegetables, fruit and other foods as tolerated. Egg yolk was added to the diet at about 6 months. Patients were supplied with evaporated milk by the case at the hospital; whole milk was delivered to them daily and viosterol was supplied at clinic visits. Assays of milk and viosterol were made from time to time to see that the vitamin D potency was constant.

1. Viosterol in oil was supplied by Mead Johnson and Co., Evansville, Ind.
2. Mead Johnson and Co.

TABLE 2.—*Comparison of Clinical Data on Feeding Groups of Infants*

Feeding Group	Infants	Males	Females	White Infants	Negroes	Months Followed (Average)	Total Visits	Weight at Birth, Gm.	Gain, Times Weight at Birth		Infections		Percentage with Clinical Rickets	Mothers with Given Classification		
									6 Mo.	12 Mo.	Total	Average		1	2	3
Breast+V5	37	16	21	30	7	12.1	446	3,480	2.2	2.73	78	2.0	76.6	30	7	0
N.I.E.+V5	42	17	25	39	3	13.3	526	3,480	2.19	2.79	131	2.4	96.3	25	12	5
E-135	53	26	27	48	5	13.6	598	3,460	2.24	2.8	125	2.4	96.0	28	13	12
E-135+V15	8	7	1	8	0	6.0	47	3,910	....	....	...	...	67.0	5	1	2
E-200	51	30	21	44	7	12 2	623	3,360	2.29	2.91	126	2.5	91.2	36	9	6
W.M.-200A	25	14	11	23	2	11.7	311	3,295	2.37	2.96	60	2.4	72.0	20	5	0
W.M.-200B	24	11	13	19	5	5.8	126	3,420	....	....	...	...	....	16	6	2
Total	240	121	119	211	29	....	2 677	.....	....	....	...	...	....	160	53	27

RESULTS

General.—Table 2 shows some general facts about the whole group. There were 240 subjects divided as indicated (infants receiving lactic acid are included). The number of male and female were about equal; the number of Negro infants was small. The infants paid a total of 2,677 visits to the clinic, averaging one a month. The birth weights

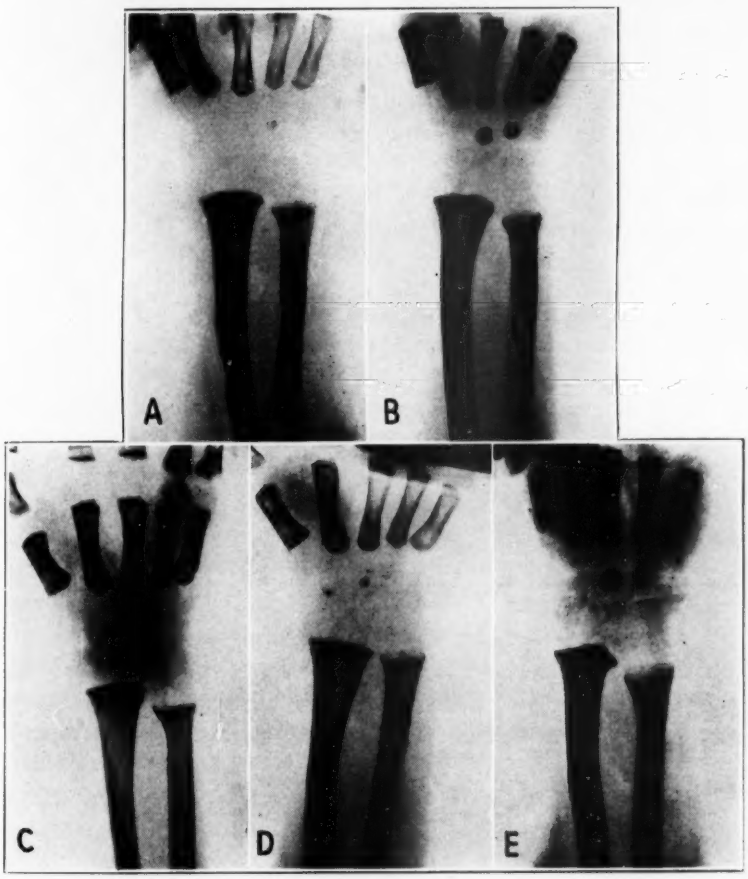

Fig. 1.—Representative roentgenograms giving evidence of rickets. In *A* the slight cupping and irregularity of the ulna is a doubtful or questionable sign of rickets. In *B* definite cupping of the ulna and in *C* flare and irregularity evidence slight rickets. In *D* moderate rickets and in *E* marked rickets are shown by the increasing irregularity, fringing and cupping of the ulna with slight changes in the radius.

for the various groups were about equal. Breast-fed infants gained a little less, infants fed on whole milk slightly more, than those on evaporated milk. In all groups each infant had more than doubled

his weight at the age of 6 months and slightly less than tripled it at 1 year.

The majority of infants appeared extremely well nourished. Most of the infections that occurred involved the upper respiratory tract—colds, otitis, pharyngitis and so on. In a few infants exanthem subitum, in a few stomatitis and in 1 or 2 mumps occurred. There were slightly fewer infections in the breast-fed than in the other groups. (The two groups of infants followed for only six months are not comparable.)

A careful check for clinical signs of rickets, such as beading, bosselation, craniotabes, flare and bowing, was made at each visit. One or more of these signs were seen in a high percentage of the infants. It was not possible to correlate these signs with the roentgenographic diagnosis of rickets. Rapoport, Stokes and Whipple [3] had the same experience. Roentgenograms must supply the final criterion.

TABLE 3.—*Comparison of Feeding Groups as to Incidence of the Various Degrees of Rickets Evidenced in Roentgenograms*

Roentgenographic Evidence of Rickets	Breast+V5	N.I.E.+V5	E-135	E-200	W.M.-200	Total	
						Number	Percentage
Negative	33	9	18	11	10	81	38.9
Doubtful	3	13	14	19	9	58	27.8
Slight	0	5	6	5	1	17	8.2
Moderate	0	5	6	8	4	23	11.0
Marked	1	10	9	8	1	29	13.9
"Negative" (N)	36	22	32	30	19	139	66.8
"Active" (A)	1	20	21	21	6	69	33.2

The last column in table 2 shows the grading of the mothers, which could easily be determined after several visits. They are classed as to the care which they gave their respective infants and the reliability of their reports. Two thirds of the mothers were in the first, or superior, class.

Rickets.—Roentgenographic evidence of rickets was seen in most cases between the third and the fifth month. The roentgenograms were graded on the standards used by Drs. Eliot and Park.[4] Representative roentgenograms are shown in figure 1.

Whenever one or more in a series of six roentgenograms showed a questionable or doubtful lesion, the patient was classed as having doubtful evidence of rickets. If one or more showed definite rachitic changes, the patient was listed as having slight, moderate or marked evidence of rickets, depending on the degree of activity shown and the

3. Rapoport, M.; Stokes, J., and Whipple, D. V.: J. Pediat. **6**:799, 1935.

4. Eliot, M. M., and Park, E. A., in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1938, vol. 1, p. 3881.

persistence. It is clear from table 3 that breast feeding plus 5 drops of viosterol in oil is most efficient in preventing rickets; whole irradiated milk is next most effective. The incidence of rickets in the entire group of infants is 33.2 per cent. The group in whom the presence of rickets was considered doubtful would be considered as not having rickets by most observers, hence they are grouped as having "Negative" (N) evidence of this disease. All the other three groups were classed together as having "Active" (A) or definite rickets. This consolidation is for the purpose of presenting other facts more concisely.

Table 4 gives additional facts about the rachitic group. There is little difference in the distribution of rickets to males and females, but the incidence in the Negro babies is much lower than that in the white ones. However, the number of Negro infants was small and most of the mothers were of a superior type.

Infections were more frequent in the rachitic group. Rachitic infants gained a little faster in the first six months. Linear growth was about equal. The figure in bold face type, in this table, is not included in the averages because it represents a case which is atypical and should be discussed separately.

Any infant breast fed for as long as three months was classed in the group of breast-fed infants, though many were given supplementary food or were weaned before the year was out. The subject just referred to was an infant breast fed up to the age of 5 months and then given nonirradiated milk with 5 drops of viosterol in oil. At 6 months this infant was below the average in weight gain; at 1 year she was above the average. Her period of growth, therefore, was during the second six months. Rickets appeared at the seventh month. Though listed as a breast-fed infant, the only actively rachitic one in that group, she probably should be considered as one receiving nonirradiated milk.

The last group of figures lists the average daily intake of milk during the first six months in the group having active rickets, in comparison with the figures for the "negative" group. In three of the four feeding groups the infants with active rickets ingested slightly less milk than those with negative evidence of the disease though they gained faster. The average intake of the infants in each group was no more than 75 per cent of the possible quart. Hence during the first six months the full unit value of vitamin D was not consumed.

Figure 2 shows the incidence of active rickets with regard to season of birth. Most of the patients were born in the first or fourth quarter, and the incidence of rickets was about the same for both these groups. Those born in the second quarter had the highest rate, 52 per cent. The numbers of cases in the groups born in this quarter and the next were relatively small. It is hard to account for the wide discrepancy in the

TABLE 4.—*Comparison of Clinical Data on Feeding Groups with "Negative" (N) and Active (A) Rickets*

Feeding Group	Males		Females		White Infants		Negroes		Infections, Average per Infant		Gain in Weight, Times Weight at Birth, 6 Mo.		Gain in Length, 6 Mo., Cm.		Ounces of Milk Daily	
	N	A	N	A	N	A	N	A	N	A	N	A	N	A	N	A
Breast+V5	16	0	20	1	29	1	7	0	2.5	...	2.23	1.89	12.8	14.2	.....	.....
N.I.E.+V5	10	7	12	13	19	20	3	0	1.9	2.7	2.14	2.28	14.5	13.7	10.05	9.73
E-135	13	11	17	10	30	18	2	3	2.3	2.5	2.18	2.23	13.8	15.6	9.68	10.14
E-200	18	12	12	9	24	20	6	1	2.3	2.6	2.16	2.28	15.2	15.1	10 02	9.63
W.M.-200	10	2	7	4	17	6	2	0	1.9	3.4	2.34	2.46	17.4	17.9	21.60	19.80
Total	71	32	68	37	119	65	20	4								
Average	..	..	..	..	..	..	..	..	2.17	2.78	2.23	2.32	15.2	15.5		

rachitic incidence in the groups born in the second and third quarters. The infants born in these quarters were all reaching the dangerous age of 3 months during the fall and winter months, when little ultraviolet radiation was available. In this connection it may be said that the mothers were not encouraged to give their babies sunbaths, but a large number reported that their babies were "outdoors all day" or several hours daily during the summer months. When definite rickets was

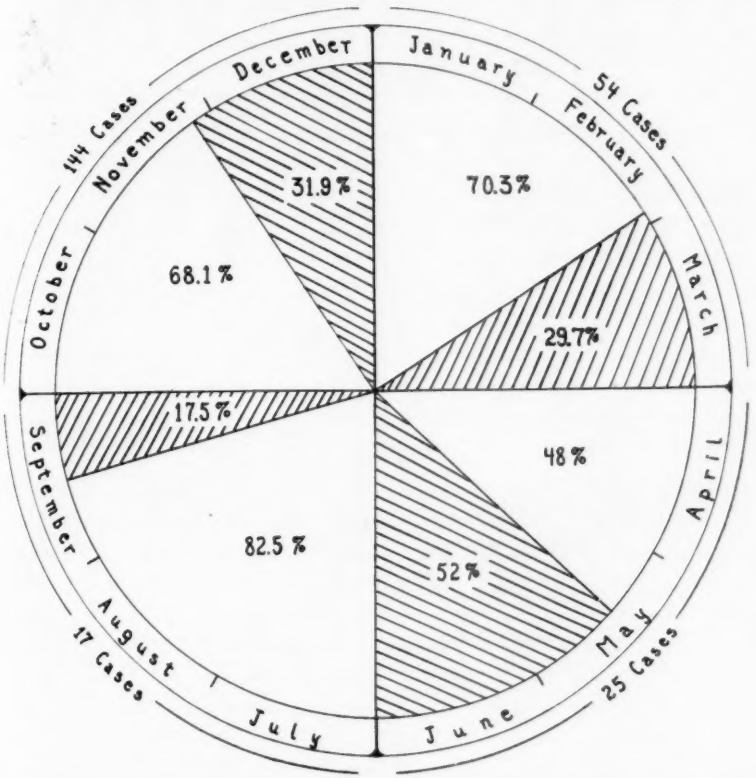

Fig. 2.—Incidence of rickets with regard to season of birth. The striped zones represent cases of rickets.

established by roentgenograms in the early spring or summer months, no additional vitamin was given, and in practically every case the rickets healed spontaneously. If the diagnosis was made in winter, vitamin was added, i. e., 15 drops of viosterol in oil, to promote healing.

In table 5 the feeding groups are considered seasonally with respect to the presence or the absence of rickets. Attention should be called to group A of the infants receiving whole milk, a group which was followed for twelve months. These babies were born in January, February and March and rickets developed in only 6 of 25.

To see how much the time of year affected appearance of rickets, a second study was started with 24 infants fed 200 unit whole milk, these infants having been born in October, November and December. Observations on a control group fed 135 unit evaporated milk plus 15 drops of viosterol in oil were started simultaneously.

A more detailed analysis of the roentgenographic evidence of rickets in these groups is shown in table 6. The incidence of rickets in the babies receiving 200 unit whole irradiated milk remained low, 4 of 24

TABLE 5.—*Influence of Season of Birth on Incidence of "Negative" (N) and Active (A) Rickets in Feeding Groups*

	January, February, March		April, May, June		July, August, September		October, November, December	
Feeding Group	N	A	N	A	N	A	N	A
Breast+V5	1	0	1	0	2	0	32	1
N.I.E.+V5	4	1	0	0	4	2	14	17
E-135	7	3	8	4	4	0	13	14
E-135+V5	0	0	0	0	0	0	6	2
E-200	7	6	3	9	4	1	14	7
W.M.-200A	19	6	0	0	0	0	0	0
W.M.-200B	0	0	0	0	0	0	20	4
Total	38	16	12	13	14	3	98	46

TABLE 6.—*Incidence of Rickets in Two Feeding Groups Comparing Infants Born in Last Quarter of Year*

	W.M.-200		E-135+V15	
Roentgenographic Evidence of Rickets	Number	Percentage	Number	Percentage
Negative	15	62.5	3	37.5
Doubtful	5	20.8	3	37.5
Slight	1	4.2	2	25.0
Moderate	1	4.2	0	0
Marked	2	8.3	0	0
Total N	20	83.3	6	75.0
A	4	16.7	2	25.0

infants. These were born in October, November and December and were followed four and a half to seven months. The control group, given 135 unit evaporated milk plus 15 drops of viosterol in oil, had more rickets than expected but all in the slight class. However, there were only 8 infants in this series, and several of the mothers were inferior, or class 3. When a mother is graded thus, one is never sure whether the infant received the added vitamin regularly.

COMMENT

The literature contains numerous conflicting reports of the efficacy of various dosages and of different types of vitamin D in the prevention of early rickets. Several reasons for these discrepancies are apparent.

In some reports the number of cases is too small to permit of statistical evaluation; in others the initial age of the infants studied is not uniform; in yet other reports too much emphasis is placed on diagnosis by clinical signs and roentgenograms are not taken frequently enough, but perhaps difference in interpretation of roentgenograms is the greatest single factor bringing about confusion.

Roentgenograms of moderately severe active or healing rickets, with obvious cupping, fringing or fresh calcium deposits, present no difficulty in diagnosis, nor do those showing an obviously normal condition. It is the roentgenogram which shows slight change from the normal, such as slight irregularity, flare or cupping, that is hard to classify. While very frequently such changes are seen in a roentgenogram preceding by a few weeks one showing active rickets, a roentgenogram with such changes may, on the other hand, be the only one to show an abnormal finding in a series of 6 roentgenograms of a single wrist. In such instances, in this study, the patient is listed as having doubtful evidence of rickets. If these changes are merely components of normal growth, as Jeans [5] suggested, it is surprising that in the breast-fed group only 3 infants, or 9 per cent, had them. Whether the roentgenograms show a normal condition or give evidence of rickets is a moot point. For the sake of clarity this group of cases in which the roentgenographic evidence for rickets is doubtful should be kept as an entity and considered as possibly presenting the earliest changes of rickets.

The influence of natural ultraviolet radiation could not be clearly shown because the number of cases was not equally distributed over the four seasons. It is important to bear in mind that in most of the cases healing of the rachitic process occurred during the summer months, without an increase in the vitamin D intake; the exceptions to this were a few cases in which active rickets appeared in the late fall. In these cases it was thought best to hasten healing by increasing the doses of the vitamin.

Rachitic babies gained on the average faster than the nonrachitic ones, but there was no appreciable difference in the rate of linear growth. At dosage levels of 400 or more U. S. P. units of vitamin D, Eliot and her associates [6] demonstrated that the infants growing most rapidly in length showed a greater tendency for rickets to develop. There was no such correlation in our patients, most of whom were maintained with a lower dosage level.

5. Jeans, P. C.: Vitamin D Milk: Relative Value of Different Varieties of Vitamin D Milk for Infants; Critical Interpretative Review, J. A. M. A. **106**:2066 (June 13) 1936.

6. Eliot, M. M.; Nelson, E. M.; Barnes, D. J.; Browne, F. A., and Jenns, R. M.: J. Pediat. **9**:355, 1936.

Other investigators, such as Stokes and Rapoport[7] and Drake, Tisdall, and Brown,[8] have found the 135 unit milk sufficient to protect against moderate and marked rickets. Our results (fig. 3) are at variance with this observation, since rickets occurred both in the group receiving milk and in that receiving 200 unit milk. Infants given homogenized whole milk had a lower incidence than those given evaporated milks at the same unit level. Viosterol in oil in the dose of 5 drops daily did not protect infants fed on nonirradiated evaporated milk, but breast-fed infants who received this same dose of viosterol were protected. The nature of this antirachitic quality of breast milk has been elusive and has not been identified; it is certainly most effica-

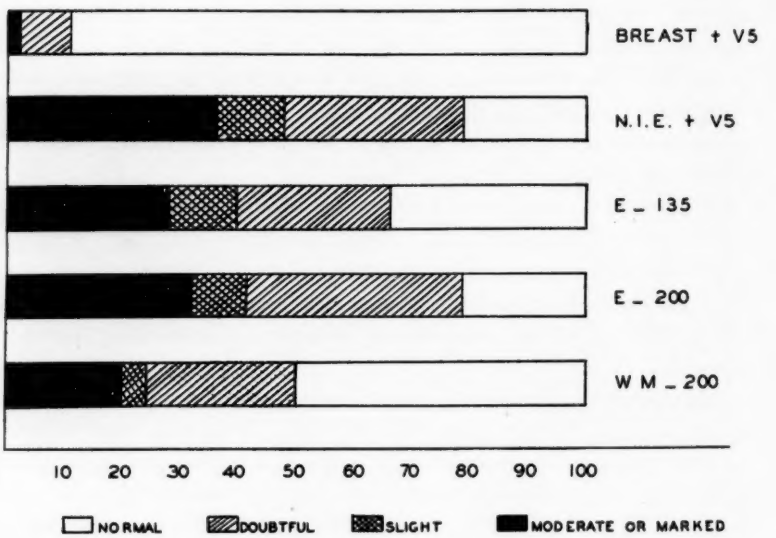

Fig. 3.—Incidence of rickets in various feeding groups.

cious and continues to be effective months after weaning. During the period of observation, in only 1 of 37 infants who were breast fed for four months or more did rickets develop after weaning.

SUMMARY

Two hundred and forty healthy infants were divided into eight feeding groups in which vitamin D was supplied from five different sources. The majority of these infants were studied for at least a year. The following observations were made:

1. Positive evidence of rickets was found in the roentgenograms in 33 per cent of the cases. In 24.9 per cent of these the appearances

7. Rapoport, M., and Stokes, J.: J. Pediat. **8**:154, 1936.
8. Drake, T. G. H.; Tisdall, F. F., and Brown, A.: J. Pediat. **6**:161, 1936.

were those of moderate or marked rickets; in 8.2 per cent, of slight rickets. In addition, in 27.8 per cent there was "questionable" evidence of rickets.

2. Breast-fed infants receiving 5 drops of viosterol in oil daily (800-1,000 U. S. P. units of vitamin D) were protected against rickets. In 1 infant bone changes of active rickets developed two months after weaning.

3. Viosterol in oil in the dose of 5 drops was not sufficient to give protection against rickets in infants fed nonirradiated milk.

4. Irradiated milk containing 135 and 200 U. S. P. units of vitamin D to the quart did not protect against rickets. Two hundred unit whole milk was more protective than 200 unit evaporated milk.

5. In most of the cases rickets healed spontaneously without increase of vitamin D during the summer months.

Case Reports

COOLEY'S SYNDROME (ERYTHROBLASTIC ANEMIA) IN A CHINESE CHILD

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ORLANDO, FLA.

Von Jaksch [1] in 1889 described a chlorotic type of anemia occurring in infancy and early childhood and accompanied by great enlargement of the spleen, hepatic swelling, leukocytosis and marked changes in the size and shape of the red blood cells. The syndrome he described became known as von Jaksch's anemia or pseudoleukemic anemia. Later a similar syndrome was described in cases of rickets, deficiency diseases, congenital syphilis, congenital hemolytic icterus and sickle cell anemia, thus discrediting von Jaksch's disease as an exact clinical entity. Many investigators felt the condition to be only a variety of secondary anemia, or, in the words of Naegeli,[2] "not a special entity but an extreme reaction." In 1925 Thomas B. Cooley, of Detroit, published with Lee an article [3] entitled: "A Series of Cases of Splenomegaly in Children, with Anemia and Peculiar Bone Changes," on a condition which occurred in patients with von Jaksch's anemia. In 1927 Cooley and his associate [4] again described this clinical syndrome, which they later called "erythroblastic anemia" [5] to signify a clinical entity. Others called the disease Cooley's anemia or Cooley's syndrome. The earliest examples occurred in members of the Mediterranean races, namely, Syrians, Greeks, Italians and Armenians. Hence in 1936 Whipple and Bradford [6] called the anemia thalassemia, or Mediterranean disease.

From the Florida Sanitarium and Hospital.

1. von Jaksch, R.: Ueber Leukämie und Leukocytose im Kindesalter, Wien. klin. Wchnschr. **2**:435, 1889.

2. Naegeli: Allgemeine Gesichtspunkte über Anämien, deren Entstehung und Einteilung, Schweiz. med. Wchnschr. **55**:1043 (Nov. 12) 1925.

3. Cooley, T. B., and Lee, P.: A Series of Cases of Splenomegaly in Children, with Anemia and Peculiar Bone Changes, Tr. Am. Pediat. Soc. **37**: 25, 1925.

4. Cooley, T. B.: von Jaksch's Anemia, Am. J. Dis. Child. **33**:786 (May) 1927. Cooley, T. B.; Witwer, E. R., and Lee, P.: Anemia in Children with Splenomegaly and Peculiar Changes in the Bones: Report of Cases, ibid. **34**:347 (Sept.) 1927.

5. Cooley, T. B., and Lee, P.: Erythroblastic Anemia: Additional Comments, Am. J. Dis. Child. **43**:705 (March) 1932.

6. Whipple, G. H., and Bradford, W. L.: Mediterranean Disease—Thalassemia (Erythroblastic Anemia of Cooley): Associated Pigment Abnormalities Simulating Hemochromatosis, J. Pediat. **9**:279 (Sept.) 1936.

CLINICAL MANIFESTATIONS

Erythroblastic anemia is a progressive disease presenting certain typical clinical features and changes in the skeletal and in the hematologic system. Onset occurs in early infancy, the symptoms usually being first noticed at the age of from 6 months to 1 year. Most of the patients whose cases are reported have been children of Mediterranean parentage. The disease apparently tends to be familial and hereditary. The following physical observations have been reported: an anemic or pale child; an undernourished and undersized child; a muddy or yellow skin; clear or slightly pigmented scleras and viscera; a large head (especially large in the parietal and the frontal region); mongoloid type of face; flattened nasal bridge; usually prominence of the cheek bones; usually cardiac hypertrophy; a protuberant abdomen, due to moderate enlargement of the liver and extreme splenomegaly; often chronic bronchitis, bronchopneumonia or other associated infection of the respiratory tract. One patient [7] had a daily elevation of temperature.

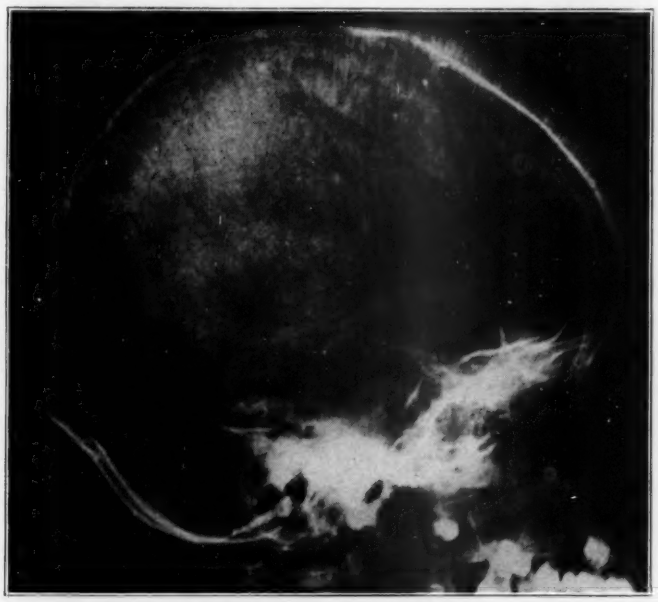

Fig. 1.—Roentgenogram of the skull of a Chinese girl with erythroblastic anemia, showing the peculiar ray formation.

Examination of the blood reveals moderate to severe anemia of the hypochromic type, a color index constantly below 1, the presence of

7. Mills, E. S.: Thalassanemia: Report of a Case, Arch. Int. Med. **62**:1004 (Dec.) 1938.

nucleated red cells varying in size and shape, reticulocytosis and, in most cases, constant leukocytosis. Basochromic stippling has been reported.

Certain tests are of some diagnostic value in erythroblastic anemia. The test for fragility of erythrocytes shows a normal or even an increased cellular resistance. The van den Bergh reaction is indirect, and the icterus index is increased.

Fig. 2.—The hands and forearms of the same patient, showing rarefaction, osteoporosity, mottling and cross striations in the bone.

The roentgenologic observations, although not pathognomonic, are striking. Changes in the skull are limited principally to the calvarium, with thickening, especially of the frontal bone, osteoporosis and cross striations (fig. 1). Usually the skull presents a peculiar ray formation due to the process of destruction of the marrow and replacement with newly formed bone. The long bones show decalcification and thinning of the cortex, with some widening of the diaphysis. The medullary portion shows irregular porosity, mottling and cross striations perpendicular and to the cortex (fig. 2).

Pathologic conditions observed at autopsy are well confined to the hemopoietic tissues and the osseous tissues and to evidences of a disordered pigment metabolism. The spleen is always large, hard and firm; microscopically it shows areas of erythroblasts, myelocytes and foam cells, with a generalized increase of connective tissue. The liver is usually enlarged, and groups of marrow cells are present in the hepatic lobules.

Fig. 3.—Appearance of the patient on admission to the hospital. Note the splenic enlargement.

REPORT OF A CASE

History.—The patient, a Chinese girl of about 6½ years, was admitted to the Waimea Hospital on June 27, 1938, with complaints of fever (temperature, 101 F.), dyspnea, general abdominal pain, occasional vomiting and a mass in the upper part of the abdomen on the left side.

Both parents were Chinese. The patient had 2 brothers and 3 sisters living and well. One sister was crippled, and another crippled sister had died from an unknown cause.

Analysis of the Blood of a Patient with Erythroblastic Anemia, Followed by an Analysis of the Blood of the Patient's Mother

Date	Red Blood Cells, Millions per Cu. Mm.	Hemoglobin, %	White Blood Cells per Cu. Mm.	Polymorphonuclears, %	Lymphocytes, %	Monocytes, %	Eosinophils, %	Basophils, %	Normoblasts, %	Stipple Cells, %	Megaloblasts, %	Microcytosis	Macrocytosis	Poikilocytosis	Anisocytosis	Achromia	Reticulocytes, %	Icterus Index	van den Bergh Reaction	Platelets, Thousands per Cu. Mm.	Coagulation Time	Bleeding Time	Comment
11/19/37	2.19	29	9,200	..	..	..	..	..	++	++	Few	..	++	++	++	..	..	..	....	...	...	...	No sign of prompt or delayed sickling of cells
12/22/37	....	..	16,000	68	30	..	2	..	Few	..	..	..	..	++	..	..	..	..	....	...	...	...	Fragility test, 0.46% to 0.38%
6/16/38	....	..	.....	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	....	...	7½	Normal	Fragility test, 0.46% to 0.38%
6/28/38	1.59	20	6,950	56	40	2	..	..	2	..	..	..	..	++	++	..	..	..	....	...	...	...	Admitted to hospital, 6/27/38; blood transfusion (150 cc.), 6/28/38
7/ 1/38	1.80	19	4,275	51	32	13	2	2	+	+	..	..	+	+	+	+	..	..	....	120	...	...	Normal fragility: upper limits = 0.44-0.42%; lower limits = 0.36-0.32%
7/ 7/38	1.75	28	8,000	53	35	10	1	1	Few	..	..	..	..	+	++	..	..	..	....	...	...	...	
10/ 2/38	....	..	.....	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	....	...	...	...	Fragility test, 0.40% to 0.28% (increased cellular resistance)
10/29/38	2.40	16	7,800	68	28	2	2	..	Few	++	++	++	..	++	++	++	1 to 2%	24	Weak indirect reaction	...	...	...	Wassermann reaction negative; patient discharged 7/27/38; last seen 12/5/38
Mother																							
10/ 2/38	4.22	52 (7.8 Gm./ 100 Cc.)	8,600	61	30	6	3	..	..	..	..	+	+	++	+	+ to few	..	..	....	...	...	...	Wassermann reaction negative

The mother stated that the child was normal at birth except that her nose was slightly more flattened than that of any of her siblings. Development was normal until the age of 5 months, when the mother first noticed a mass in the upper part of the abdomen on the left side. Anemia appeared shortly thereafter and had been present, with occasional partial remissions, ever since. The mass had grown steadily larger. During the first few years, until the child came to Waimea Hospital as an outpatient, she was not under a doctor's care.

Physical Examination.—The patient (fig. 3) appeared somewhat stunted in growth both mentally and physically as compared with her brothers and sisters. Her blood pressure was 112 systolic and 70 diastolic. The temperature was 99 F., the pulse rate 100 and the respiratory rate 20. There was severe orthopnea. The complexion was pale and had an icteric tinge. The frontal bone and cheek bones were prominent and thickened in appearance. She had a saddle nose. The mongoloid features were more exaggerated than in the siblings. The scleras appeared slightly icteric, the pupils reacted to light and in accommodation, and the hearing was good. There were several carious teeth, and the upper jaw was prominent. The tongue was clean, and the throat normal. The tonsils were moderately hypertrophied.

The heart was greatly enlarged, extending almost to the left anterior axillary line. A loud systolic mitral murmur was heard over the apex. Examination of the lungs showed normal fremitus, no dulness and normal breath sounds. The abdomen protruded, especially on the left side. It showed no scars. The liver was moderately enlarged and tender. The spleen was greatly enlarged and extended from the diaphragm to below the level of the umbilicus. The extremities were thin and anemic. Neurologic examination showed the reflexes to be normal.

Microscopic Examination.—The analysis of the blood is outlined in the table. It revealed profound chlorotic anemia. Smears showed constantly nucleated achromic red cells, with poikilocytosis and anisocytosis. Megaloblasts and macrocytes were reported in some of the smears. The icterus index was 24, and the van den Bergh test positive (delayed direct reaction). There were a low platelet count and a reticulocyte count of 1 to 2 per cent. The first two tests for fragility were negative, and the third showed somewhat increased cellular resistance. Leukocytosis was not constant. The Wassermann test was negative. Sickle cells were never noted.

Examination of the blood of the patient's mother on Oct. 2, 1938 showed moderate chlorotic anemia, with a red cell count of 4,220,000, 52 per cent hemoglobin (7.8 Gm., 100 cc.) and a color index of 0.64. The white cell count was 8,600. Smears showed microcytes, macrocytes, a few achromic cells, anisocytosis and extreme poikilocytosis, with a reticulocyte count of 1 per cent. The result of the test for fragility was normal. The Wassermann reaction was negative, and roentgenograms showed slight changes in the skull. The father and the brothers and sisters had normal blood counts.

COMMENT

This is the first case of erythroblastic anemia in a Chinese of which I can find any report. It is likewise one of the few cases reported in which the patient was not of one of the Mediterranean races. The mother has moderate anemia of the same type and a suggestive roentgen picture. This is interesting, since erythroblastic anemia has been considered hereditary. The mother may have a low grade of erythroblastic anemia. The patient did not have as constant or as high a

leukocytosis as has generally been reported. This, however, is not inconsistent with a diagnosis of Cooley's anemia, as others (Mills [7] and Sendrail, Lyon and Lasserre [8]) have noted the same condition.

Erythroblastic anemia has long been considered a familial or hereditary disease; however, the basis for this belief has not always been well substantiated. In the case here reported the patient's mother shows symptoms consistent with a diagnosis of low grade erythroblastic anemia. Cases of similar familial involvement, in which the syndrome occurred in adults, have been reported recently by Aravantinos and Delijannis [9] and Allen and Childs.[10] Usually the pathologic changes observed in an adult are not as marked as they are in a child.

In 1932 Cooley and Lee [5] stated: "We are not inclined . . . to lay great stress on the limitation of this or any other similar disease to a particular race." I have seen reports of a case of the disease in a Hindu child [11] and a case of it in an English child.[12] In the case reported here it occurs in a Chinese child. These instances of the disease in persons not of the Mediterranean races and other, similar instances which will be encountered should lead one back to the original name for this syndrome—erythroblastic or Cooley's anemia.

NOTE.—Since preparing this paper I have received a letter from Dr. Kenneth Amlin, of Waimea, Kauai, stating that this patient died some time in the spring of 1939. The patient's age at the time of death was 7 years. Permission for autopsy was not obtained.

My former associate Dr. Burt O. Wade, of Waimea, Kauai, Territory of Hawaii, saw the patient with me and helped in collecting the bibliographic references.

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8. Sendrail, M.; Lyon, A., and Lasserre, J.: Infantilisme splénique de type Cooley, Bull. et mém. Soc. méd. d. hôp. de Paris **52**:902 (June 8) 1936.

9. Aravantinos, A., and Delijannis, G.: Ueber das Auftreten der Erythroblastenanämie bei Erwachsenen, Klin. Wchnschr. **15**:1792 (Dec. 5) 1936.

10. Allen, E. G., and Childs, D. S.: Erythroblastic Anemia, New York State J. Med. **36**:641 (April 15) 1936.

11. Mukherji, M.: Cooley's Anemia (Erythroblastic or Mediterranean Anemia), Indian J. Pediat. **5**:17 (Jan.) 1938.

12. Bywaters, E. G. L.: Cooley Syndrome in an English Child, Arch. Dis. Childhood **13**:173 (June) 1938.

BROMIDE INTOXICATION

ITS OCCURRENCE IN A CHILD OF FOUR YEARS

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In spite of the extensive use of the bromides in the therapy of children, the case of severe bromide intoxication here presented is unique [1] in the experience of my associates and me at the Children's Memorial Hospital, and only 1 other case of a similar condition in a child under 13 years has been found in the literature. This offers a striking contrast to the many instances of bromide intoxication in adults reported in recent years. The case is recorded in the hope that it may serve both as a warning and as an incentive to further observations along these lines. Attention is especially directed to the profound psychic and neurologic changes, with which there was a complete absence of the commonly more well known cutaneous lesions.

REPORT OF CASE OBSERVED

A 4 year old girl was admitted to service of Dr. Joseph Brennemann on Nov. 14, 1938. One was immediately struck by the bewildering and apparently ominous clinical picture. There was apparently a complete stunning of the child's psyche. She stared into space oblivious to her environment; if her attention could be gained, it was not held; she uttered a few unintelligible words and speech was accomplished with great difficulty, as if there was extreme effort both in thought and in execution. Especially remarkable were the motor changes. The child, even when lying in bed, had constant rhythmic movements of the hands, arms, head and trunk. The movements were not increased or stopped by voluntary motion. Such motion produced marked symmetric ataxia in all extremities. When an attempt was made to get her to stand she collapsed in a heap. The implications were even more startling when the mother said that the "sickness" had progressed rapidly to its present picture in a period of less than two weeks.

The child had had two moderately severe attacks of asthma in the past five months, the last about two weeks ago. There seemed to have been definite changes in her behavior in the past month, and she had become extremely nervous and excitable. A difficulty in walking had developed and had progressed to a marked staggering. She had recently become disoriented and seemed "unable to control her voice." The mother stated that nervousness and insomnia had persisted despite the administration of sedatives.

Physical examination otherwise gave essentially negative results. The pupils were equal and reacted promptly to light. The fundi were normal. The super-

From the Children's Memorial Hospital.
Read before the Chicago Pediatric Society, March 21, 1939.

1. See addendum.

ficial reflexes were sluggish but equal. Plantar responses were normal. There was no evidence of involvement of cranial nerves. A tentative diagnosis of possible midline cerebellar tumor, abscess of cerebellum or encephalitis was made. In view of the history of sedation and the unusual clinical picture, bromide intoxication was suggested at this time, but the parents did not know the nature of the sedative and little credence was given to the possibility.

The parents were then asked to inquire as to the composition of the sedative which had been given, and it was found that a phenobarbital-bromide mixture consisting of ¼ grain (0.016 Gm.) of phenobarbital and 15 grains (0.96 Gm.) of sodium bromide to the drachm (3.88 Gm.) had been prescribed in the dosage of 1 drachm four times daily. Hence, the child had been receiving 60 grains (3.8 Gm.) of sodium bromide and 1 grain (0.064 Gm.) of phenobarbital per day for the past five months. The nursemaid was said to have given "an extra dose or two" during periods of extreme restlessness or insomnia. An attempt was made to find out the primary reason for giving the sedative. Apparently it was first administered because of a mild "nervousness." The parents said that recently the child had had spells of not paying any attention when spoken to at the toilet. However, this was after she had been given the phenobarbital-bromide mixture for some time and was already speaking thickly.

The child was seen by a neurologist, whose observations were essentially the same as have already been presented. He felt that the diagnosis lay between tumor or degenerative disease in the region of the mesencephalon and that the former was the more likely. He considered bromide intoxication as a remote possibility.

The erythrocytes averaged about 3,500,000 and the leukocytes 12,000, with a normal differential count. Routine examination showed the urine to be normal except for an occasional leukocyte. The results of the Kolmer, Eagle and Kahn tests were negative. Roentgen examination of the skull, chest and long bones showed them to be essentially normal.

Determination of the blood bromide concentration on Nov. 17, 1938 revealed 353 mg. per hundred cubic centimeters. The result of the qualitative test for bromides in the urine was strongly positive.

Sodium chloride in a dose of 20 grains (1.28 Gm.) four times daily, with as much salt as was tolerated in the diet, was started on Nov. 17, 1938, and there was gradual but immediate improvement. The child became more alert and conscious of her surroundings. She began to talk somewhat more freely, although somewhat haltingly. The coarse tremor began to disappear, and the ataxia was much less marked. Within five days she could walk alone with some support. Four days after administration of sodium chloride had been started the blood bromide concentration dropped from 353 mg. per hundred cubic centimeters to 214 mg., and the blood chloride concentration at this time was 528 mg. per hundred cubic centimeters.

The child became lonesome and was allowed to go home. However, at home she was extremely restless and did not sleep, so she was readmitted to the hospital after one day. The general picture was much the same except that now she seemed to be having hallucinations and would stare off into space as if listening to somebody or would move her lips as if speaking. During these periods she would immediately respond and answer questions if spoken to. In one instance she seemed to be apprehensive and talked of "being in an attic full of ladders." The blood bromide concentration at this time was 62 mg. per hundred cubic centimeters and the blood chloride concentration was 452 mg. Subsequent deter-

minations of the bromide concentration showed a less rapid but a continuous drop, with the chloride concentration remaining relatively the same. The last determination, made on Dec. 10, 1938, showed a bromide concentration of 33 mg. and a chloride concentration of 412 mg. The result of the qualitative test for bromides in the urine was no longer positive.

By Dec. 15, 1938, about one month after the first admission to the hospital, the child was apparently almost her normal self, except that when walking she seemed to throw her feet forward and to slap them down a little more than is natural. She was dicharged from the hospital at this time.

The child has not been seen since the time of discharge, but the following letter was received from her father on Jan. 12, 1939. "At first she was restless at night, showed some jealousy of the baby, wet the bed and was irritable. In the past week to ten days we have noticed a very marked improvement, and she's now seldom restless at night, hasn't wet the bed in a couple of weeks, likes the baby more than ever and has returned to her former good-humored self. She walks well, although not perfectly. She does not stagger at all, but shows some imperfection in handling her feet at times. This is getting better right along. She is very wide awake, alert in speech and actions, friendly and playful. In general, her health is the best it's been at any time since she was born."

REPORT OF THE CASE IN THE LITERATURE

As already mentioned, we have found only 1 report of the occurrence of bromide intoxication in a child. This report was made by Gralka [2] in 1924 and is extremely interesting.

Gralka reported a sudden, simultaneous occurrence in a family of 5 adults and 2 young children of a peculiar condition, characterized in the adult first observed by extreme somnolence, slovenliness, loss of memory, mental disorientation, inability to walk or write correctly and involuntary evacuation of urine and feces. The 4 other adults, seen later, presented practically the same symptoms. One child, 1¾ years of age, paid no attention to its environment, clung to its mother, was dizzy, staggered, clutched at support and fell if not held. It was formerly a very active child and spoke freely, but now it was hardly able to utter a few words inarticulately and disconnectedly. The younger child, an exclusively breast-fed infant, was abnormally sleepy. After two weeks in the hospital all the patients were apparently well. Bread was the only article of diet common to all except the infant. The family had formerly used bread from a bakery but recently had been making bread in the home. Rats fed on the bread presented symptoms similar to those in the adults and died within the first two weeks. Within a few days after returning home all of the family were sick, exactly as before. Again bread was the only article common in the diet. A different flour had been used this time, and rats fed with this flour throve. However, rats fed on the salt that had been used in making the bread all died as before. The salt was then analyzed and found to contain 5.1 per cent sodium chloride and 72.7 per cent sodium bromide. The father was a druggist, and because of inability to buy salt somebody from the family had gone to the drug store to get it and had evidently drawn on the sodium bromide receptacle, which stood next to the one that contained sodium chloride. The infant had evidently ingested sodium bromide excreted in the mother's milk.

2. Gralka, R.: Akute Massenvergiftung mit Bromnatrium: Endemisch aufgetretene, nicht infectiöse Schlafsucht, Klin. Wchnschr. **3**:319 (Feb. 19) 1924.

COMMENT

Bromide intoxication has been presented as a definite clinical entity with increasing frequency during the past ten years. However, the majority of reports have been from psychiatric services or institutions and almost all of the patients have been adults. It apparently has hardly been considered as a pediatric problem. Of course, the use of bromide as a therapeutic agent for children is not so widespread as its use for adults. In many of the cases, intoxication in adults has occurred through the taking of a patent medicine over a long period, yet in not a few it has resulted through the taking of a drug prescribed by the attending physician. Also, adults have often taken the medicament or had it prescribed for some primary psychoneurotic condition, and hence the symptoms of bromide intoxication served only to complicate the clinical picture or to overshadow the underlying pathologic process.

In 1850, about ten years after the introduction of the bromides as therapeutic agents, the first case of bromide intoxication was reported by Huette.[3] After this there were but occasional reports until those of Wile [4] and Wuth [5] in 1927. Since then the syndrome has been recognized and reported much more frequently. Hanes and Yates [6] recently reported a study of 400 cases of chronic bromide intoxication. They stated that in a six and one-half year period at Duke Hospital, Durham, N. C., abnormal amounts of bromide were demonstrated in more than 700 patients, or in approximately 0.9 per cent of the total number admitted. Harris and Hauser [7a] in 1930 cited the fact that of 500 patients consecutively admitted to the Colorado State Psychopathic Hospital 7 per cent had bromide intoxication.

The occurrence of bromide intoxication is rather easily explained. The total halogen content of the body is relatively constant and normally is almost entirely composed of chlorides. The chlorides are maintained at a nearly constant level by the ability of the body to excrete excess chlorides. When the bromide ion is introduced it tends to replace the

3. Huette: Recherches sur les proprietes physiologiques et therapeutiques de bromure de potassium, Mém. Soc. de biol. **2**:19, 1850.

4. Wile, U. J.: Bromide Intoxication: Further Studies, J. A. M. A. **89**:340 (July 30) 1927.

5. Wuth, O.: Rational Bromide Treatment: New Methods for Its Control, J. A. M. A. **88**:2013 (June 25) 1927.

6. Hanes, F. M., and Yates, A.: An Analysis of Four Hundred Instances of Chronic Bromide Intoxication, South. M. J. **31**:667 (June) 1938.

7. (*a*) Harris, T. H., and Hauser, A.: Bromide Intoxication: Its Significance in Toxic and Delirious States, J. A. M. A. **95**:94 (July 12) 1930. (*b*) Frugoni, P., and Walsh, M. N.: Bromide Psychosis, Proc. Staff Meet., Mayo Clin. **12**:125 (Feb. 24) 1937. (*c*) Cross, W. D. S.: Bromide Intoxication, Canad. M. A. J. **35**:283 (Sept.) 1936.

chloride ion. The rate of excretion of the bromide ion is relatively slow as compared with that of the chloride ion. Hence there is an accumulation of the bromide ion in the body. This accumulation may obviously be enhanced by a decrease in the intake of sodium chloride in the diet, by dehydration or by an alteration in the rate of excretion of the bromide, as in disease of the kidney. The level of blood bromide concentration when toxic manifestations occur has arbitrarily been set at 150 mg. per hundred cubic centimeters, with individual variations.[7] Fatal cases have been reported by Wagner and Bunbury,[8] and more recently a case by Barbour, Pilkington and Sargant,[9] in which the blood bromide concentration was 500 mg. per hundred cubic centimeters.

The symptoms of bromide intoxication, while varied, present a fairly definite clinical syndrome. The onset is rather insidious; often the first thing noted is an unusual hyperexcitability, and, ironically, the bromide medication is often increased to counteract this. There are a slurring of speech, an uncontrollable generalized tremor, and difficulty in walking because of a marked ataxia. There may be hallucinations, both auditory and visual. If intoxication is severe there may be stupor, or even coma and death. Swallowing may be difficult and the mucous membranes dry. The pupils may be unequal and react sluggishly to light. Superficial reflexes may be absent and deep reflexes diminished. There may or may not be an elevation of temperature. It is apparently relatively uncommon to find evidence of a rash. This is an important point, as in the absence of the characteristic cutaneous lesions one is even more likely to overlook the possibility of the bromides as being the cause of the psychic and neurologic changes.

The diagnosis may be extremely confusing, not so much because of a variability in the symptoms as because the possibility of bromide intoxication is not considered. The symptoms may suggest encephalitis, intracranial neoplasm or Tay-Sachs disease. A history of bromide medication should suggest the diagnosis of bromide intoxication, and this diagnosis is easily established by determination of the bromide concentration in the blood[10] or may be suggested by the detection of bromides in the urine.[11]

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8. Wagner, C. P., and Bunbury, D. E.: Incidence of Bromide Intoxication Among Psychotic Patients, J. A. M. A. **95**:1725 (Dec. 6) 1930.

9. Barbour, R. F.; Pilkington, F., and Sargant, W.: Bromide Intoxication, Brit. M. J. **2**:957 (Nov. 14) 1936.

10. Katzenelbogen, S., and Goldsmith, H.: The Hemato-Encephalic Barrier: The Diagnostic Value of the Bromide Test in Mental Diseases, Am. J. Psychiat. **10**:1045 (May) 1931. Katzenelbogen, S., and Czarski, T.: Improved Colorimetric Method for Determination of Bromide Concentration in Blood and Cerebrospinal Fluid, Proc. Soc. Exper. Biol. & Med. **32**:136 (Oct.) 1934.

11. Todd, J. C., and Sanford, A. H.: Clinical Diagnosis by Laboratory Methods, Philadelphia, W. B. Saunders Company, 1937.

The treatment is primarily that of replacing the accumulated bromide ion by the chloride ion in abundant amounts. Sodium chloride may usually be administered orally. In the case presented 20 grains (0.96 Gm.) of sodium chloride taken four times a day with as much salt as tolerated in the diet was effective. The salt was given in capsules containing 5 grains each and was taken without difficulty. In cases of severe intoxication, when oral administration is not satisfactory, injection of physiologic solution of sodium chloride by the subcutaneous or the intravenous route is indicated. Drinking of fluids should be urged. Although there were moderate restlessness and insomnia in our case, no sedatives were given. It is mentioned by various authors that in the treatment of the restlessness and insomnia associated with bromide intoxication sedatives are in general unsatisfactory, and Cheavens, Carter and Bagwell [12] were probably right in stating that "the withdrawal of all sedatives is in the long run the best procedure."

One may well wonder whether the diagnosis of chronic bromide intoxication is not occasionally overlooked, especially with milder degrees of the condition. Thus Hanes and Yates [6] described the picture of mild chronic bromide intoxication in adults and showed that symptoms of intoxication often appear in such patients with a blood bromide concentration of even less than 100 mg. per hundred cubic centimeters. It seems obvious that one should at least have the possibility of such intoxication in mind when bromides are prescribed for a long time or in large doses for children, especially if for any reason chlorides are not taken or retained in normal amounts.

SUMMARY

A case of bromide intoxication in a 4 year old girl is reported. Accompanying profound psychic and neurologic changes yielded fairly promptly to withdrawal of bromides and free administration of sodium chloride.

ADDENDUM

Since this paper was presented, a second case of bromide intoxication has been observed at the Children's Memorial Hospital.

C. T., a 3¼ year old girl, had been followed in the neurology clinic since February 1937 because of epileptiform convulsions. The condition had been fairly well controlled with phenobarbital until August 1938, when she was given ½ grain (0.032 Gm.) of sodium diphenyl hydantoinate dilantin N. N. R. twice a day. Convulsions immediately became more frequent and severe; so the use of sodium diphenyl hydantoinate was discontinued and phenobarbital was again prescribed. In Novem-

12. Cheavens, T. H.; Carter, C. F., and Bagwell, J. S.: Mental Disturbances Due to Bromide Intoxication: Clinical Study of Twenty-Three Cases, Texas State J. Med. **33**:375 (Sept.) 1937.

ber 1938 the child was admitted to the hospital because of a severe infection of the upper respiratory tract and made an uneventful recovery. She was seen in the neurology clinic Jan. 11, 1939, and a prescription containing approximately 15 grains (0.96 Gm.) of sodium bromide to the drachm (3.88 Gm.) was ordered in the dosage of 1 drachm three times daily. She was again seen March 1, 1939, but nothing unusual was noted. Her next visit was April 19, 1939, and at this time the mother said that for the past four months the child had not been as active as usual. Her appetite had seemed to fail. She appeared to keep her eyes half closed, and friends had asked why she looked so tired. Her legs seemed weak, so much so that she "had to hold on to things when walking about." In the past month her gait had been definitely staggering, and in the past week she had been unable to walk without falling. She seemed more irritable and slept poorly. Her speech seemed to be "slow." No evidence of a rash had been noted.

The blood bromide concentration was then found to be 480 mg. per hundred cubic centimeters. She was admitted to the hospital. The results of physical examination were negative except for gross tremor of the tongue, arms and legs, marked ataxia, moderate ptosis and inarticulate speech. The skin was clear. There were no signs of increased intracranial pressure. The urine showed a positive reaction for bromides. Laboratory data were otherwise essentially negative. As in the first case, a diet rich in sodium chloride and also 5 grains (0.19 Gm.) of sodium chloride in capsules three times a day were given. In fourteen days the blood bromide concentration had dropped from 480 mg. per hundred cubic centimeters to 69 mg. The coarse tremor had disappeared, and the child could walk fairly well, although she was still somewhat unsteady. She had become more alert and her speech normal. She could feed herself without difficulty. She was discharged from the hospital May 6, 1939, and was again seen in the outpatient department May 10, 1939, at which time the blood bromide concentration was 45.4 mg. per hundred cubic centimeters and the child was apparently her normal self.

707 Fullerton Avenue.

SO-CALLED CONGENITAL IDIOPATHIC HYPERTROPHY OF THE HEART

BEN BENJAMIN, M.D.
AND
MORRIS A. SIMON, M.D.
MONTREAL, CANADA

A survey of the literature reveals that under the heading "congenital idiopathic hypertropy of the heart" numerous pathologic conditions are included. In some of the cases the cause for the hypertrophy is known and therefore the cardiac enlargement should not be identified as "idiopathic." To this group in particular belong the cases of glycogen storage disease,[1] cases of enlargement of the heart associated with hypertension[2] and cases of enlargement accompanying severe anemia.[3] In a much larger number of cases, while the etiologic factors are not absolutely established, cardiovascular abnormalities and/or pathologic changes are reported which could have some causal relation to the cardiac hypertrophy. This group comprises cases in which there are anomalies of the great vessels,[4] abnormalities of the origin and distribution of the coronary arteries,[5] rhabdomyomas,[6] myocardial degeneration and pericardial, endocardial and perivascular fibrosis.[7]

From the Department of Pediatrics and the Pathological Laboratories of the Jewish General Hospital.

1. (*a*) van Creveld, S.: Glycogen Disease, Medicine **18**:1, 1939. (*b*) Humphreys, E. M., and Kato, K.: Glycogen Storage Disease, Am. J. Path. **10**:589, 1934.

2. Mussliner, S.: Beitrag zur sogenannten idiopathischen Herzmuskelhypertrophie und zur essentiellen Hypertonie im Kindesalter, Ztschr. f. Kinderh. **50**:134, 1930.

3. Tung, C. L.; Bien, W. N., and Chu, Y. C.: The Heart in Severe Anemia, Chinese M. J. **52**:479, 1937. Ball, D.: Change in the Size of the Heart in Severe Anemia, with Report of a Case, Am. Heart J. **6**:517, 1931.

4. (*a*) Stoloff, E. G.: So-Called Idiopathic Enlargement of the Heart in Infancy and in Childhood, Am. J. Dis. Child. **36**:1204 (Dec.) 1928. (*b*) Kugel, M. A., and Stoloff, E. G.: Dilatation and Hypertrophy of the Heart in Infants and in Young Children, with Myocardial Degeneration and Fibrosis (So-Called Congenital Idiopathic Hypertrophy), ibid. **45**:828 (April) 1933. (*c*) Abbott, M. E., in Nelson Loose-Leaf Living Medicine, New York, Thomas Nelson & Sons, 1931, vol. 4, p. 207.

5. Carrington, G. L., and Krumbhaar, E. B.: So-Called Idiopathic Cardiac Hypertrophy in Infancy, Am. J. Dis. Child. **27**:449 (May) 1924. Bland, E. F.; White, P. D., and Garland, J.: Congenital Anomalies of the Coronary Arteries:

(Footnotes continued on next page)

It is with a case of the latter type, one in which profound endocardial fibrosis and moderate perivascular and epicardial fibrosis as well as irregular hypertrophy of the fibers occurred, that the following report is concerned.

REPORT OF A CASE

History.—An Irish-Canadian infant, a girl 4 months old, was admitted to the pediatric service of the Jewish General Hospital on the night of Nov. 24, 1938, because of restlessness, vomiting and coughing. The mother and father were well. They had had 2 children before this one; the first was stillborn and the second was a girl, 4 years old, who was well. The patient was born at term after a normal pregnancy and normal delivery. Her weight at birth was 6 pounds 12 ounces (3,062 Gm.). The neonatal period was uneventful. After the usual loss of weight the infant regained her birth weight by the time she was 10 days old. She was breast fed with complemental feedings for the first three weeks, after which the mother's milk disappeared. The infant did not thrive. The feedings were taken poorly, thirty minutes usually being required for only 2 ounces (59 cc.). The most the baby ever took was 4 ounces (118 cc.) at a feeding. Mixtures using evaporated milk as well as some using fresh cow's milk were tried. Vomiting was a predominant feature from early life. It was not projectile, and the vomitus did not contain bile. Viosterol drops were given daily, as well as orange juice, which was only occasionally retained. The child cried a great deal. No definite cyanosis was noticed. There was considerable coughing without signs of a cold. Twenty-four hours prior to the child's admission to the hospital, the coughing, vomiting and restlessness had increased.

Physical Examination.—The infant was normally developed but undernourished (weight, 10 pounds 2 ounces [4,593 Gm.]; length, 25 inches [63.5 cm.]) and rather flabby. She was irritable and slightly dyspneic when at rest. The lips and finger nails showed some cyanosis. There was no clubbing of the fingers or toes. The skin presented a somewhat waxy appearance. The throat was moderately reddened. Over the left posterior half of the chest there was dulness, and the breath sounds were diminished but not bronchial. No rales or friction rub was heard. The area of cardiac dulness was enlarged to the right and to the left. The heart beat was rapid and regular, and the sounds were not considered abnormal. No murmurs or pericardial friction rub was heard. The liver and the spleen were not enlarged. The blood pressure was 98 mm. of mercury systolic and 40 mm. diastolic. The red blood cell count was 3,900,000 per cubic millimeter, and the hemoglobin content, 76 per cent (Hellige). The white blood cell count was 14,000 per cubic millimeter, with a differential count of 71 per cent polymorphonuclears (20 per cent immature and 51 per cent segmented), 26 per cent lympho-

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Report of an Unusual Case Associated with Cardiac Hypertrophy, Am. Heart J. **8**:787, 1933.

6. Virchow, R.: Verhandlungen ärztlicher Gesellschaften, Berl. klin. Wchnschr. **33**:679, 1896. Farber, S.: Congenital Rhabdomyoma of the Heart, Am. J. Path. **7**: 105, 1931. Wegman, M. E., and Egbert, D. S.: Congenital Rhabdomyoma of the Heart Associated with Arrhythmia, J. Pediat. **6**:818, 1935.

7. (*a*) Mahon, G. S.: Idiopathic Hypertrophy of the Heart with Endocardial Fibrosis, Am. Heart J. **12**:608, 1936. (*b*) Powers, G. F., and LeCompte, P. M.: Remarks on a Case of Congenital Idiopathic Hypertrophy of the Heart, J. Pediat. **13**:760, 1938. (*c*) Stoloff.[4a] (*d*) Kugel and Stoloff.[4b]

cytes, 2 per cent large mononuclears and 1 per cent eosinophils. The urine was light amber colored and acid, contained a trace of albumin but no sugar and on microscopic examination showed only a few pus cells. A roentgenogram of the chest revealed an enormous heart shadow, which could have been cast either by an extremely enlarged heart or by a massive pericardial effusion (fig. 1). The pulmonary fields were clear.

Course.—On November 25 at 9 p. m. cyanosis, dyspnea and restlessness suddenly became extreme. Although the infant remained in an oxygen tent continuously thereafter, the cyanosis did not disappear nor did her condition improve. She died at 8 a. m. the next day. During the thirty-five hours she had been in the hospital,

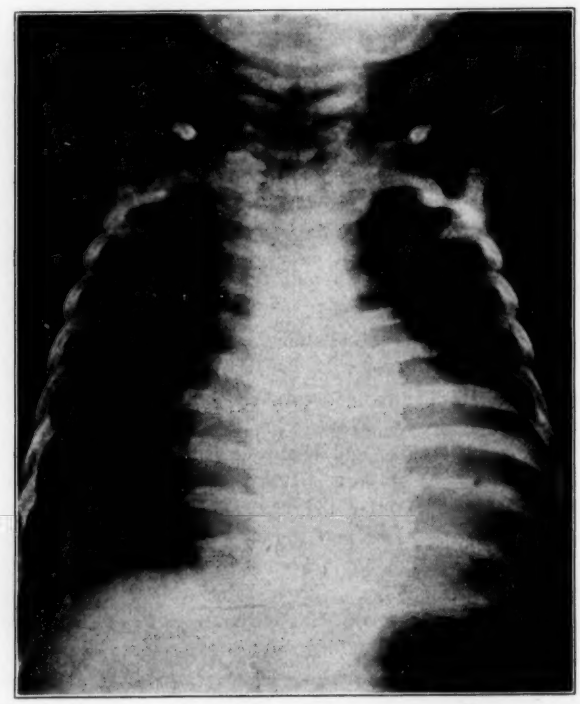

Fig. 1.—Roentgenogram showing a tremendous increase in the size of the cardiac silhouette.

the temperature (rectal) had ranged between 99.6 and 101.8 F., the pulse rate from 100 to 160 + per minute and the respiratory rate from 40 to 92 per minute. The diagnosis was congenital idiopathic hypertrophy of the heart and atelectasis of the lower lobe of the left lung.

Autopsy.—Autopsy was performed ten hours after death. The body had been kept in a refrigerator at 4 C. for nine hours. A portion of the left ventricular myocardium was immediately fixed in absolute alcohol.

The thymus weighed 23 Gm. On section it was fleshy, and a few bright red, punctate hemorrhages less than 1 mm. in diameter were seen.

The striking feature consisted in the tremendous increase in the size of the pericardial sac and its contents, the apex of which touched the left thoracic wall

in the midaxillary line. The entire lower lobe of the left lung lay behind the heart and was the seat of compression atelectasis. The pericardial sac contained 10 cc. of clear, straw-colored fluid which was sterile on culture, as was the heart's blood.

The heart was greatly enlarged in all diameters, weighing 97 Gm., as opposed to the normal weight of 27 to 30 Gm. for an infant of that age (Coppoletta and Wolbach[8]). Everywhere the epicardium was slightly thickened and somewhat opaque, and over the anterior surface a roughly circular, milky plaque 1.5 cm. in diameter was seen. The auriculoventricular sulcus was obliterated by fibrous adhesions which were covered by epicardium (fig. 2).

On section all the chambers of the heart were seen to be increased in size, and the trabeculae carneae were thick and flattened. The endocardium on the right side of the heart was only slightly thickened, but on the left it was gray

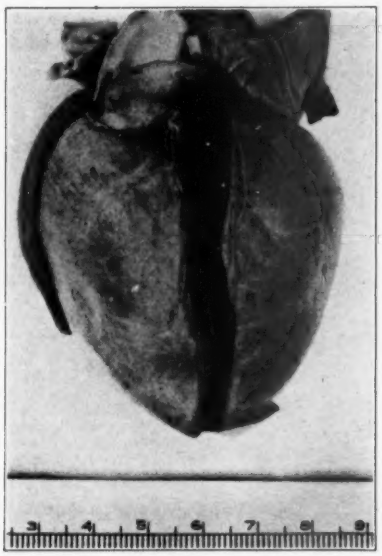

Fig. 2.—Lateral view of the heart, showing extreme globular hypertrophy (weight, 97 Gm.). Note the thickening and opacity of the epicardium.

and opaque and in some places as much as 1 mm. thick. The valve leaflets, while slightly thickened, were pliable, smooth and translucent and showed no anomalies. The foramen ovale was sealed, and there were no septal defects. The myocardium was red, firm and thickened in both ventricles (fig. 3).

The ductus arteriosus was patent to a probe and was anomalous in that it opened into the systemic aorta at the level of, and opposite, the left subclavian artery. At this point the aorta was slightly constricted owing to a subintimal ridge about the circumference. The coronary arteries were patent and showed no anomalies in size, origin or distribution. No gross pathologic changes were present. The other organs were not remarkable grossly.

8. Coppoletta, J. M., and Wolbach, S. B.: Body Length and Organ Weights of Infants and Children, Am. J. Path. **9**:55, 1933.

Sections taken from various portions of the heart were fixed in diluted (10 per cent) solution of formaldehyde U. S. P., made neutral, and were then stained with hematoxylin and eosin, Mallory's connective tissue stain, Van Gieson's stain and Weigert's elastic tissue stain. The alcohol-fixed material was stained for glycogen by Best's carmine method.

Microscopically, multiple sections taken from various portions of the left ventricle showed in all preparations tremendous fibrous thickening of the endocardium. This fibrous tissue was relatively acellular and occasionally dipped deeply into the underlying myocardium. In some places the thickened endocardium appeared as concentrically lamellated whorls on the ventricular surface (fig. 4).

In the myocardium there was moderate perivascular fibrosis, and in one situation a few histiocytes were seen in perivascular position. There was a slight but definite increase in the fibrous connective tissue throughout the myocardium. In

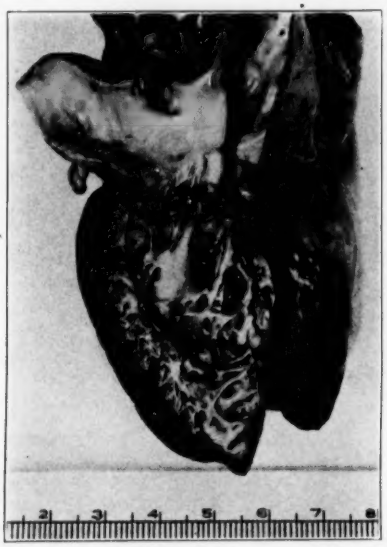

Fig. 3.—Heart sectioned to show the thickness of the left ventricle, thickening and flattening of the trabeculae carneae and gray, opaque, thickened endocardium. Note that the mitral valve is uninvolved and that the fibrosis of the endocardium extends into the left ventricle.

no situation, however, was evidence of active inflammation present (fig. 5). The myocardial fibers were unequal in width, some showing squaring of the nuclei. Two hundred myofibrils were measured. Only fibrils lying free and easily identifiable as single fibers were measured at the level of the nucleus. Variation in diameter from 5 to 15 microns was found.

Sections of the thickened endocardium stained by Weigert's method showed a slight increase of elastic fibers in the endocardium, many of which were fragmented.

Multiple sections taken through the left auricle showed changes similar to those described in the left ventricle but to a lesser degree, while sections from the right ventricle showed similar changes that were only minimal. Sections of the alcohol-fixed myocardium stained by Best's carmine method and ptyalin controlled showed

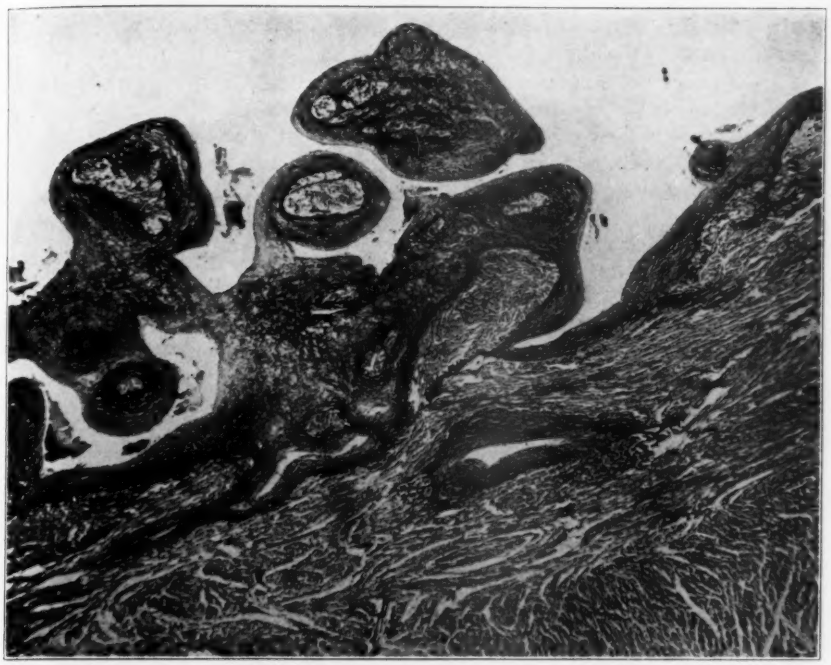

Fig. 4.—Photomicrograph showing tremendous thickening of the endocardium. Note the whorling of endocardium in the upper right hand corner and the dipping of the fibrous tissue into the underlying myocardium. (Mallory's stain for connective tissue; low power.)

Fig. 5.—Photomicrograph showing perivascular fibrosis in the myocardium. (Mallory's stain for connective tissue; medium power.)

only a few small red-staining granules, and these were mainly in the modified neuromuscular (Purkinje) fibers directly underneath the endocardium. This was considered physiologic.

Sections of the lungs showed considerable dilatation of the blood vessels and engorgement of the capillaries, with well preserved red blood cells. A number of phagocytes filled with golden brown, granular pigment were seen within the alveoli, but no exudate was present. Section of the lower lobe of the left lung showed compression atelectasis.

Except for a few small petechiae in the thymus gland the remaining organs were not remarkable histologically.

Autopsy showed definite pathologic changes involving the endocardium, myocardium and epicardium. It is entirely conceivable that these changes could result from a nonspecific low grade pancarditis.

COMMENT

Congenital idiopathic hypertrophy of the heart has been defined by Abbott [9] as a condition which is "characterized by great cardiac enlargement in the absence of any sign of myocardial disease or other intra- or extracardiac etiologic factor, a pure or primary hypertrophy of the muscle fibers alone existing."

In a review of the literature up to 1933, Kugel and Stoloff [4b] pointed out that of 52 collected cases only 17 were found which could conceivably fulfil the conditions of the foregoing definition. They described 7 additional cases in which evidence of myocardial inflammation and endocardial and perivascular fibrosis were associated with hypertrophy. In 1934, Levine [10] added another case similar to the case reported here. In 1936, Mahon [7a] contributed 2 more cases that fit into this category, and recently Powers and LeCompte [7b] added another.

It is therefore evident that by far the greatest number of cases of cardiac hypertrophy in infants is associated with definite pathologic changes in the heart. These changes either are inflammatory or show the residua which usually result from inflammatory changes. Certainly in the presence of these pathologic changes the hypertrophy cannot be considered "idiopathic" even though we may not be able at the moment to point to the etiologic agent. The possibility that these pathologic changes are the result of intrauterine infection or of infection unrecognized during the early days of life cannot be excluded, in spite of the absence of evidence in the histories. If unrecognized infection may occur in early postnatal life, the resulting hypertrophy may not be, strictly

9. Abbott, M. E.: Atlas of Congenital Cardiac Disease, New York, The American Heart Association, 1936, p. 26.

10. Levine, H. D.: Cardiac Hypertrophy in Infancy Associated with Thickened Endocardium and Coarctation of the Aorta, Am. J. Dis. Child. **48**:1072 (Nov.) 1934.

speaking, congenital. That the type and degree of the pathologic changes just described are in themselves sufficient cause for hypertrophy cannot be definitely stated in any given case. Experimentally Eyster [11] has shown that only cardiac injury which has led to dilatation is sufficient stimulus for the production of persistent hypertrophy.

Lewis [12] has shown that the heart responds promptly (within two or three months) to an increased load. Such an increased load may devolve on myocardial fibers which have remained uninjured when a certain number have been destroyed by inflammation. Through inflammation a heart may become dilated, and this then could be the stimulus for hypertrophy.

The hypertrophy of the fibers in the present case was quite irregular, some fibers being three times thicker than others. The length of the fibers was also irregular, but this was not measured. According to Dammin and Moore,[13] the first response of a heart undergoing hypertrophy in infancy is an increase in the length of the fibers. This process is irregular and does not parallel the increase in their width. Although these investigators found no increase in the number of nuclei, they do not exclude the possibility of hyperplasia, as suggested by McMahon.[14] No mitosis or evidence of hyperplasia of myocardial fibers was seen in this instance. Although the thymus was large, there were no pathologic conditions to support a diagnosis of so-called status thymicolymphaticus, which, as Vischer [15] has shown, probably plays no part in the development of cardiac hypertrophy. There was no history of hypertension in the parents of this infant, and the evidence presented by Mussliner [2] suggesting that so-called idiopathic hypertrophy rests on a constitutional basis requires further proof.

The presence of the small amount of glycogen which was demonstrated in our case is physiologic. No large granules or excessive focal deposits of glycogen were seen. No vacuolation was observed in the preparations stained with hematoxylin and eosin.

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11. Eyster, J. A. E.: Cardiac Dilatation and Hypertrophy, Tr. A. Am. Physicians **42**:15, 1927. Eyster, J. A. E.; Meek, W. J., and Hodges, F. J.: Cardiac Changes Subsequent to Experimental Aortic Lesions, Arch. Int. Med. **39**:536 (April) 1927. Eyster, J. A. E.: Experimental and Clinical Studies in Cardiac Hypertrophy, J. A. M. A. **91**:1881 (Dec. 15) 1928.

12. Lewis, T.: Diseases of the Heart, ed. 2, New York, The Macmillan Company, 1937, p. 118.

13. Dammin, G. J., and Moore, R. A.: Cardiac Muscle in Idiopathic Hypertrophy of the Heart in Infancy and in Normal Growth, Arch. Path. **27**:122 (Jan.) 1939.

14. McMahon, H. E.: Hypertrophy of the Heart in Infants, Am. J. Dis. Child. **55**:93 (Jan.) 1938.

15. Vischer, M.: Beiträge zur Myokarditis im Kindesalter, Berlin, S. Karger, 1924, pt. 2.

Recently abnormal glycogen metabolism as a cause of cardiac enlargement has, perhaps, been overemphasized. This would seem to be a comparatively rare occurrence. While a special cardiomegalic type of glycogen storage disease has been described,[16] it must be recognized that this type of abnormal metabolism does not result in cardiomegaly in all cases.[17] Furthermore, the carmine-staining granules or vacuoles observed histologically in the musculature of restudied hearts which were earlier reported as being affected with so-called idiopathic hypertrophy are not sufficient proof to warrant calling the condition cardiomegalia glycogenica, as has been done by Pompe,[18] Putschar,[19] Bischoff [20] and Finkelstein.[21]

The clinical course in our case fits in with the characteristic description reported by others. Refusal of feedings, restlessness, vomiting, coughing and failure to thrive are the prominent features. Terminally, dyspnea and cyanosis appear rather suddenly and are soon followed by death. Careful physical examination reveals enlargement of cardiac dulness but no adventitious sounds. The abnormality of the heart may go unrecognized for some time. In this instance the infant had been examined in three different pediatric outpatient clinics between the ages of 1 and 3 months, and no cardiac abnormality was detected. This may conceivably be explained by the tendency on the part of clinicians to associate cardiac disease in infants with the presence of murmurs and in their absence to omit any further examination of the heart.

The dulness and diminution of breath sounds at the base of the left lung due to compression atelectasis may lead to an erroneous diagnosis of pneumonia. Fever is usually present in the terminal stage, though it may be slight, as in this instance. The leukocyte count is within normal limits or slightly elevated. The pulse rate is not persistently rapid until shortly before death.

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16. Antopol, W.; Heilbrunn, J., and Tuchmann, L.: Enlargement of the Heart Due to Abnormal Glycogen Storage, Am. J. M. Sc. **188**:354, 1934. van Creveld.[1a]

17. von Gierke, E.: Hepato-Nephromegalia glykogenica (Glykogenspeicherkrankheit der Leber und Nieren), Beitr. z. path. Anat. u. z. allg. Path. **82**:497, 1929. Unshelm, E.: Die Glykogenkrankheit, Jahrb. f. Kinderh. **137**:257, 1932. Faber, V.: Ueber die Glykogenkrankheit, Frankfurt. Ztschr. f. Path. **47**:443, 1935.

18. Pompe, J. C.: Hypertrophie idiopathique du cœur, Ann. d'anat. path. **10**: 23, 1933.

19. Putschar, W.: Ueber angeborene Glykogenspeicherkrankheit des Herzens, "Thesaurismosis Glycogenica" (von Gierke), Beitr. z. path. Anat. u. z. allg. Path. **90**:222, 1932.

20. Bischoff, G.: Zum klinischen Bild der Glykogenspeicherkrankheit (Glykogenose), Ztschr. f. Kinderh. **52**:722, 1932.

21. Finkelstein, L. E.: Cardiomegalia Glycogenica Circumscripta, Am. J. M. Sc. **191**:415, 1936.

This condition has been reported in newborn infants (Abbott [4c]). Most of the patients succumb during the first year (Kugel and Stoloff,[4b] Abbott [4c]).

SUMMARY

A case of hypertrophy of the heart in a 4 month old infant is described. The heart showed massive endocardial fibrosis, epicardial thickening and adhesions and perivascular fibrosis—a picture which could result from a healed, low grade, nonspecific pancarditis.

It is suggested that a critical attitude toward cardiac hypertrophy in infancy may lead to a clearer understanding of the pathogenesis of what has heretofore been called "congenital idiopathic hypertrophy."

News and Comment

GENERAL NEWS

Courses in Child Development and Parent Education.—The usual summer courses in child development and parent education at the University of Iowa will be from June 8 to August 2 this year.

UNIVERSITY NEWS

University of Buffalo.—Dr. William J. Orr has been made professor and head of the department of pediatrics of the School of Medicine, University of Buffalo.

Northwestern University.—Dr. Stanley Gibson has been made head of the department of pediatrics at the Medical School of Northwestern University, on the retirement of Dr. I. A. Abt.

SOCIETY NEWS

American Public Health Association.—The sixty-ninth annual meeting of the American Public Health Association will be held in Detroit from Oct. 8 to 11, 1940.

DEATHS

Dr. M.-L. Condat, professor of clinical pediatrics and puericulture at the University of Toulouse, France, died recently, at the age of 53 years.

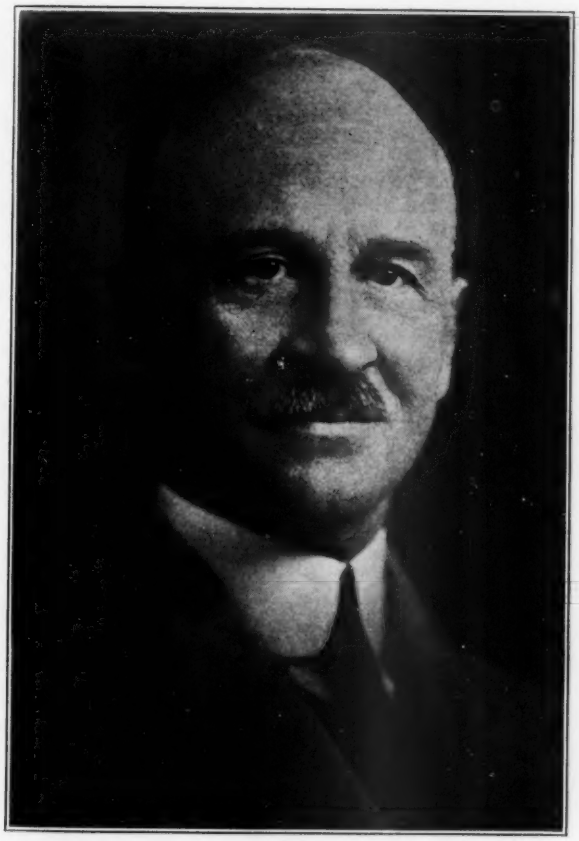
CORRECTION

In the review of "Congenital Malformations," by Douglas P. Murphy, in the March issue (AM. J. DIS. CHILD. **59**:682, 1940), the price is given as $1.50. It should read "$2.00."

Obituaries

DAVID MURRAY COWIE, M.D.
1872-1940

Dr. David Murray Cowie lived a distinguished life as clinician, scientific investigator and teacher of medicine. He was born in Moncton, New Brunswick, Canada, in 1872, of sturdy Scotch medical ances-



DAVID MURRAY COWIE, M.D.
1872-1940

try, and died on Jan. 7, 1940, at Ann Arbor, Mich. He received his medical degrees from the University of Michigan and the University of Heidelberg. He founded the department of pediatrics in the University of Michigan in 1906 and became professor of pediatrics in the medical

school in 1920, retaining that position until his death, at which time he held the title of chairman of the department of pediatrics and infectious diseases. In 1912 he established the well known Cowie Hospital, a private institution, in which he died.

Dr. Cowie was a member of numerous national and international medical and scientific societies, and his widely sought advice on matters pertaining to medicine brought him into the official service of many of them. Notably, he served for several years as member of the council of the American Pediatrics Society, and he became president of this society in 1923. He made important contributions to medical literature. In addition to his numerous articles on pediatric subjects, which require no cataloguing here, his researches were numerous in the diversified fields of internal medicine, clinical laboratory procedures, allergy, immunity, metabolism, nutrition and bacteriology. He also collaborated in such textbooks as Cecil's and served on various editorial boards, including that of the AMERICAN JOURNAL OF DISEASES OF CHILDREN. His wide interests were shown in his membership in historical societies, in his deep concern in child welfare groups and in his activities in procuring legal enactments safeguarding the well-being of children in his state. Notable was his initiative in establishing the Iodized Salt Commission in Michigan, the efforts of which produced marked diminution in the incidence of endemic goiter in that state and elsewhere.

As important as were these activities on the part of Dr. Cowie, he no doubt has left his greatest impress as a teacher of medicine and a trainer of pediatricians. Many outstanding practitioners and investigators in pediatrics in this country were inspired to devote their activities to the care of infants and children by the teaching and example of Dr. Cowie. His personal interest in his associates and his efforts in behalf of their professional advancement, together with his unselfish traits of personality, endeared him to them and stimulated in return a devoted loyalty on their part. His clear thinking, his unremitting zeal, his keen scientific insight, his resourcefulness and his liberality of thought and expression deeply influenced his co-workers. The high standards he inculcated in them will leave an indelible impression on American pediatrics.

D. J. L.

Obituaries

DEWITT H. SHERMAN, M.D.
1864-1940

Pediatrics has lost one of its pioneers. Dr. Dewitt H. Sherman died on February 1 of aplastic anemia. His death brought to a close a career that was closely linked with the development of pediatrics in this country; in western New York the progress of his specialty during the past half-century is blazed with the milestones of his achievements.

Dr. Sherman was born in Buffalo and received his early education in that city. In 1886 he was granted the degree of Bachelor of Arts from Williams College. He graduated from the Medical School of the University of Pennsylvania in 1890 and one year later from the University of Buffalo School of Medicine. After an internship at the Episcopal Hospital in Philadelphia, Dr. Sherman laid the groundwork for his specialty by studying for the next year in Berlin, Germany. On his return to Buffalo he began private practice and at that time became actively associated with the University of Buffalo School of Medicine, in the department of therapeutics. Later he became professor of this department.

In 1909 he established the department of pediatrics at the university, and for the first time this specialty enjoyed a place of its own in the medical school. He was awarded the post of professor of pediatrics at this time and held this position until 1929, when he retired and was designated emeritus professor of pediatrics. During his stewardship of twenty years as professor, he was unswerving in his efforts to improve the quality of teaching, to build up his department and to demonstrate that pediatrics played a most important role in the medical curriculum. At the time of his retirement, it must have been most gratifying to him to know that he had achieved his goal and that his department had risen from the position of a nonentity to become one of the strongest in the medical school.

Coincident with the progress of pediatric teaching at the medical school, Dr. Sherman's progressiveness and ability as a teacher and organizer was felt at the Children's Hospital, for it was through his guidance and public spiritedness that this institution grew from a sixteen bed to a two hundred and fifty bed hospital. Like other progressive educators of his day, he also appreciated the importance of clinical bedside instruction. Early in his career he encouraged a close affiliation

between the school and the hospital. After his retirement as chief of service in pediatrics, Dr. Sherman still maintained an active interest in teaching by serving as director of postgraduate education. He held this position until a few years before his death.

Dr. Sherman was at one time president of the Erie County Medical Society. He was one of the organizers of the section of pediatrics in the New York State Medical Society and served as fourth chairman of the section. In the New York State Department of Health he served as regional consultant in pediatrics. In 1914 he was elected a member of the American Pediatric Society; he was vice president in 1938-1939 and editor of the semi-centennial volume in 1939. He was a founder member of the American Academy of Pediatrics.

Nothing can better portray his sterling qualities and his devotion to the cause of medical education than the announcement which followed soon after his death that he had given the bulk of his estate to the University of Buffalo Medical School. Mrs. Sherman has since generously added to the bequest of her husband, and there is now available a fund of half a million dollars for the erection of a new medical school building.

To the hundreds of his students and friends, his loss will leave a void that will never be filled, but we who were fortunate enough to have known him will always cherish the memory of his kindly spirit, which was ever young and indomitable, his generosity, his humanitarianism and his modest evaluation of his own admirable traits—marks of a truly great man.

W. J. O.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

Detection of Colonies of Pneumococci and Streptococci on Blood Agar by Dried Bile. P. H. Greey, J. Infect. Dis. **64**:206 (May-June) 1939.

Sometimes it is difficult and inconvenient to perform bile solubility tests. Greey describes a simple method in which merely dropping dried bile on the bacterial colonies on blood agar results in the dissolving out of the pneumococci. The colonies of Streptococcus viridans and Streptococcus haemolyticus still remain. This seems a practical test.

Toomey, Cleveland.

Reaction of Lymphatic Tissue of Rabbits to Repeated Injections of Bacterium Monocytogenes. E. A. Conway, J. Infect. Dis. **64**:217 (May-June) 1939.

Bacterium monocytogenes when injected into a host always calls forth the characteristic monocytosis. Conway describes the events which take place in the first forty-eight hours after reinjection of the cultures into rabbits which had been previously immunized to this bacterium. He describes these changes at length.

Toomey, Cleveland.

Survival and Death of Tubercle Bacilli Subjected to Oxygen Restriction. T. S. Potter, J. Infect. Dis. **64**:261 (May-June) 1939.

Potter reports that human, like avian, tubercle bacilli may survive prolonged drastic deprival of oxygen at 37 C. Avian tubercle bacilli, like the human tubercle bacilli studied by Novy and Soule, are unable to survive a relatively mild restriction of oxygen at 37 C. when such restriction is combined with accumulation of the gaseous products of their metabolism on glycerin agar.

Toomey, Cleveland.

Use of Experimental Pneumonia in Rats for the Evaluation of Therapeutic Procedures. W. J. Nungester and A. H. Kempf, J. Infect. Dis. **64**: 288 (May-June) 1939.

Nungester and Kempf produced pneumonia in rats, and the lesions paralleled closely the conditions encountered in man at the time when treatment is instituted. Although specific immune serum decreased the mortality from the disease and the incidence of pleurisy, there was nevertheless an appreciable mortality.

Toomey, Cleveland.

Presence of Avian Tubercle Bacilli in Apparently Pure Cultures of Diphtheroids. J. McCarter and E. G. Hastings, J. Infect. Dis. **64**:297 (May-June) 1939.

McCarter and Hastings isolated several species of diphtheroids from bovine and porcine lymph nodes. The cultures when inoculated into experimental animals produced avian tuberculosis. However, purified cultures of the diphtheroids did not produce tuberculosis. Both avian bacilli and diphtheroids grow commensally, and the growth of the tubercle bacillus cannot be detected macroscopically. They are both present in the same culture, and the assumption cannot be made that the culture is pure and that the diphtheroid is a phase in the life cycle of the acid-fast organism.

Toomey, Cleveland.

BACTERICIDAL AND GROWTH-INHIBITORY EFFICACY OF MONOVALENT SATURATED ALCOHOLS. U. P. KOKKO, Arch. f. Hyg. **122**: 44 (April) 1939.

The author employed in his experiments the so-called suspension method on Bacillus coli and Staphylococcus aureus. He demonstrated that the disinfecting power of the alcohols increases according to the increasing number of straight carbon chains in the molecule, whereas among the isomers of an equal number of carbon atoms it decreases, following the order: primary normal > iso-alcohol > secondary alcohol > tertiary alcohol.

Irrespective of the number of carbon atoms and their order in the molecule, the bactericidal and growth-inhibitory efficacy of these alcohols rises in accordance to the height of their boiling point. FALKENHEIM, Rochester, N. Y.

DETERMINATION OF CREATINE AND CREATININE. E. C. NOYONS, Nederl. tijdschr. v. geneesk. **83**:2595 (June 3) 1939.

A quantitative method is described for estimating creatinine and creatine in urine and for estimating creatinine in blood serum. On comparing the various methods of determining creatinine in biologic fluids, Noyons found the creatinine figures indicated in literature to be much too high. This must be ascribed in part to the use of insufficiently purified trinitrophenol, to impurity of the creatinine used as a standard for colorimetry, to the insufficient removal of substances disturbing the determination, which usually results in figures too high, and to the use of a common colorimeter instead of an apparatus for absolute colorimetry. VAN CREVELD, Amsterdam, Netherlands.

Metabolism; Infant Feeding; Milk and Other Foods

THE EFFECT OF PROTEIN AND EXERCISE AT DIFFERENT AGES ON THE TOTAL ENERGY METABOLISM. ALEX BLACK and J. R. MURLIN, J. Nutrition **17**: 347 (April) 1939.

By means of a direct-indirect automatic calorimeter the total energy metabolism of albino rats from weaning to the age of 8½ months was determined as affected by proteins at levels of 8 and 20 per cent of whole milk powder and dried whole egg (equicaloric rations). One half of the animals on the 20 per cent protein ration received a mild amount of exercise. The authors called attention to the superiority of egg protein over milk protein for growth production. The level of protein intake did not influence heat production. The average total metabolism was the same for the three groups on milk rations; it was somewhat lower for those on the egg rations except in the exercised group.

FREDEEN, Kansas City, Mo.

THE EFFECT OF PROTEIN AND EXERCISE AT DIFFERENT AGES ON THE BASAL METABOLISM. ALEX BLACK, J. Nutrition **17**:361 (April) 1939.

Black found that the basal heat production for young rats averaged lowest in the group on a diet low in protein (8 per cent) and highest in the group given a high protein (20 per cent) diet plus exercise. A higher basal metabolic rate was noted in old rats with a high protein intake. Old rats as compared to young showed higher basal metabolic rates. FREDEEN, Kansas City, Mo.

A QUANTITATIVE STUDY BY MEANS OF SPECTROGRAPHIC ANALYSIS OF ALUMINUM IN NUTRITION. FLORENCE J. SCOULAR, J. Nutrition **17**:393 (April) 1939.

Scoular made thirty-five studies of aluminum balance with 3 normal preschool boys and concluded that aluminum is not an essential constituent of the diet. FREDEEN, Kansas City, Mo.

THE IMPORTANCE OF DEFICIT OF SODIUM AND CHLORIDE IN DEHYDRATION. DANIEL C. DARROW, J. Pediat. **13**:670 (Nov.) 1938.

Two cases are presented to illustrate that the central feature of the syndrome called dehydration is loss or deficiency of sodium and chloride. A 3 year old boy with an extensive burn had symptoms of acidosis and salt deficit after spending sixty of sixty-four hours in a tub containing hypotonic salt solution. Improvement resulted after continuous infusion with hypertonic solution of sodium chloride and sodium bicarbonate. The second case was that of a 7½ month old baby with diarrhea and signs and symptoms of dehydration. Marked decrease in concentration of total bases in the serum was found on the child's admission to the hospital. After administration of sodium chloride and sodium bicarbonate, negligible amounts were excreted in the urine and in the stool, and the retention of large amounts of sodium and chloride was not accompanied by a gain in weight. Recovery from all symptoms and signs of dehydration occurred within twenty-four hours. In the first case loss of sodium chloride resulted from diffusion of extracellular electrolytes from the tissue spaces and capillaries into the hypotonic salt solution in the tub. No loss of water occurred, but the signs and symptoms of dehydration were due to shift of extracellular water into the cells. The infant with "intestinal" intoxication was also not suffering from loss of total "body water" but from dehydration of extracellular fluids and increased hydration of intracellular fluids due to loss of sodium and chloride. Darrow, using these 2 cases as examples, discusses the treatment of dehydration.

RAUH, Cincinnati.

EFFECT OF GELATINE ON MUSCULAR FATIGUE. G. B. RAY, J. R. JOHNSON and M. M. TAYLOR, Proc. Soc. Exper. Biol. & Med. **40**:157 (Feb.) 1939.

These investigators trained 6 men and 4 women on an ergometer until the maximal output of work before fatigue set in was constant. They then gave the subjects 45 to 60 Gm. of gelatin (which contains 25 per cent aminoacetic acid) in fruit juice each day and measured the output of work before fatigue set in. In the men they noted 37 to 240 per cent increases above the output of the training period, but in the women they observed no appreciable increase. After the gelatin was discontinued but the fruit continued the output of work rapidly fell to the previous levels. It seemed as though this effect was particularly concerned with the creatinogenic action of the amino acids, especially that of aminoacetic acid.

HANSEN, Minneapolis.

ACID BASE BALANCE AND THE DISTRIBUTION OF FAT IN THE BLOOD. R. LEVINE and SAMUEL SOSKIN, Proc. Soc. Exper. Biol. & Med. **40**:305 (Feb.) 1939.

A reciprocal relationship has been demonstrated between the carbon dioxide–combining power of the blood and the concentration of total fat in the blood serum. No change was noted in the fat content of whole blood, the increase in the serum fat being due to a shift of fat from the red blood cells to the plasma. This may have some significance as regards fat transport from foodstuffs to the tissue cells.

HANSEN, Minneapolis.

SUPPRESSION OF LACTATION BY ORAL ŒSTROGEN THERAPY. G. L. FOSS and P. PHILLIPS, Brit. M. J. **2**:887 (Oct. 29) 1938.

This article cannot be abstracted. It must be read in its entirety to be appreciated. However, the authors arrive at the conclusion "that oestrone acts specifically on the mammary gland, in some way preventing the action of the lactogenic hormone of the anterior pituitary, or even by a direct antagonism to this lactogenic hormone. At present an explanation of this clinical finding cannot justifiably be ventured. It is unlikely that such small doses will in any way influence the chemical constitution of human milk."

ROYSTER, University, Va.

GLUTATHIONE CONTENT OF THE BLOOD IN ACUTE AND CHRONIC NUTRITIONAL ILLNESSES OF INFANTS. A. RACUGNO, Lattante **10**:17 (Jan.) 1939.

The method for determining the glutathione content of the blood was that of Forleo. In 13 cases of acute gastroenteritis, the amount of glutathione content of the blood tended to be above normal. This increase is interpreted as a reaction of the body toward greater consumption of oxygen to meet the need of increased metabolism in the tissues. In the majority of 9 cases of chronic nutritional disturbance (atrophy) the glutathione level was below normal. Therefore, for both these conditions sulfur-containing products are logical therapeutic agents.

HIGGINS, Boston.

EXPRESSION OF MOTHERS' MILK AND ITS USE IN INSTITUTIONS FOR INFANTS. D. MOGGI, Riv. di clin. pediat. **37**:324 (April) 1939.

The pediatric clinic at Florence has developed since 1933 a service for collection of mothers' milk. This expressed breast milk has proved of value for three groups of infants: (*1*) premature and immature infants; (*2*) atrophic infants whose mothers have no milk or insufficient milk and infants with severe infection, such as pneumonia, and (*3*) infants with gastroenteritis. Moggi cites 52 cases in which this service was of value.

HIGGINS, Boston.

SO-CALLED "NORMAL LEAD" IN COW'S MILK AND IN MILK PREPARATIONS. M. KASAHARA, S. NOSU, R. KAWAMURA and H. FUJII, Jahrb. f. Kinderh. **147**:357 (Oct.) 1936.

Figures are given for raw, sterilized, skimmed and pasteurized milk. Small quantities of lead were present in all. Numerous tables of values are given.

LANDAU, Hannibal, Mo.

ASCORBIC ACID CONTENT OF BREAST MILK IN SUMMER AND IN WINTER. H. WINKLER and E. HEINS, Ztschr. f. Geburtsh. u. Gynäk. **117**:148 (April) 1938.

The investigations of the authors show that colostrum has a lower vitamin C content than breast milk and that the vitamin C content of colostrum in winter is lower than in summer. It increases from the first to the fifth day post partum and reaches a fairly constant level; in winter it is about one-third lower than in summer. With greater parenteral intake of vitamin C the content is raised to a certain level, beyond which it cannot be increased; this rise is faster in summer than in winter. The authors conclude that lack of fresh fruit and vegetables causes a deficiency in vitamin C in winter and that this vitamin should be administered to pregnant women during the winter months. Addition of vitamin C to the diet in summer is unnecessary if the diet is well selected.

ADAIR and POTTER, Chicago.

Vitamins; Avitaminoses

VITAMIN B DEFICIENCY AND NERVOUS DISEASES. F. H. LEWY, J. Nerv. & Ment. Dis. **89**:174 (Jan.-Feb.) 1939.

This is an excellent review of the subject of neuritis. The thesis is based on a critical analysis of 164 references, supplemented by a study of many clinical cases. Lewy concludes that regardless of the clinical form of the neuritis in the individual case the histologic change is basically uniform: It is a cloudy swelling gradually progressing to Waller's degeneration. The intermediary link, Lewy postulates, is in the liver. In many metabolic, toxic and infectious processes the liver cells become depleted of their stores of glycogen and simultaneously of their vitamin B. As soon as more than one third of the mobile stock of vitamin B in

the liver has been exhausted, the fixed depot of the nervous system begins to decrease and the first nervous symptoms make their appearance in the form of increased electrical irritability of the peripheral nerves.

JAHR, Omaha.

HYPOVITAMINOSIS A IN SCHOOL CHILDREN. L. CAUSSADE, NEIMANN C. THOMAS and DAVIDSOHN, Rev. franç. de pédiat. **14**:209, 1938.

The authors discuss various tests for vitamin A deficiency and describe a relatively simple one used by them in testing a group of school children. The child is introduced into a dark room, and during two minutes he regards a well lighted screen, after which he is left for thirteen minutes in absolute dark. After this he regards a screen on which letters are delimited with progressively increasing light. The least light with which these are distinguished is regarded as the threshold. Fifteen children free from hepatic and ocular disturbances were used for establishing the normal. In school children, particularly of the poor classes, a considerable incidence of hypovitaminosis A was found.

LESLIE, Evanston, Ill.

THE CAROTENOIDS AND VITAMIN A OF THE BLOOD. S. W. CLAUSEN and A. B. MCCOORD, J. Pediat. **13**:635 (Nov.) 1938.

Studies are reported to call attention to the more important factors which affect the level of the carotenoids and of vitamin A in the blood: placental transmission, diet, infection, age and season and the effect of certain morbid states (diabetes, Bright's disease, celiac disease and hypothyroidism). Large amounts of carotene and xanthophyll may pass through the placenta to the fetus. Vitamin A probably also passes through the placenta, but the fetus may be able to form vitamin A from carotene. Normal infants and older persons readily absorb carotene from the diet, but the rate of absorption is slower than the rate of absorption of vitamin A. The low carotenoid content of the diet in early infancy and in the winter months explains the lower concentration of carotene and xanthophyll in the first six months of life and in the winter. The mean vitamin A concentration of the plasma in normal persons reaches a constant level soon after birth and is not affected by season. Infection, due partly to low intake and partly to fever, causes a prompt fall in the concentration of carotene, xanthophyll and vitamin A in the plasma. The vitamin A content of the plasma may rise above normal a few days after the temperature becomes normal. Xanthosis cutis in normal persons, in diabetic persons and in persons with hypothyroidism is associated with an increase of carotene in the plasma (less often, of xanthophyll). In severe untreated diabetes the tissues may not be able to metabolize carotene rapidly. In nephrosis and in severe chronic nephritis, hypercarotenemia may occur without xanthosis cutis. In Bright's disease the vitamin A level of the plasma may be partly elevated, probably because the liver fails to store it. In hypothyroidism the carotenoids of the plasma may be elevated and vitamin A may be low. Treatment with thyroid substance corrects this anomaly. In celiac disease the carotenoids and vitamin A are not readily absorbed.

RAUH, Cincinnati.

THE EFFECT OF VITAMIN D ON LINEAR GROWTH IN INFANCY: II. THE EFFECT OF INTAKES ABOVE 1,800 U. S. P. UNITS DAILY. P. C. JEANS and GENEVIEVE STEARNS, J. Pediat. **13**:730 (Nov.) 1938.

The rate of linear growth of 9 infants given from 1,800 to 4,600 units of vitamin D daily has been compared with standard rates of growth and with the growth of infants treated with the same dietary regimen but with amounts of vitamin D varying from 135 to 340 units daily. The rate of growth of infants receiving the largest number of units of vitamin D was similar to or less than that of infants given 135 units daily and definitely lower than that of infants given 340 units of vitamin D daily. It is concluded that the effect of vitamin D on increase of linear growth reaches a maximum when the intake of vitamin D is

greater than 135 and less than 1,800 units, probably in the neighborhood of 340 to 600 units, daily. Vitamin A in amounts exceeding those of the food apparently does not affect the linear growth of infants. RAUH, Cincinnati.

TOPICAL APPLICATION OF VITAMIN A (EFFICIENCY JUDGED BY GROWTH STIMULATION). WALTER H. EDDY and JOAN L. HOWELL, New York State J. Med. **39**:406 (March 1) 1939.

Absorption of vitamin A through the skin was studied in rats. Applications of the vitamin product were made to the back of the neck after skin had been clipped from the area. It was found that both carotene and vitamin A are absorbable by intact rat skin in sufficient amount to stimulate growth. Carotene is better absorbed than vitamin A. AIKMAN, Rochester, N. Y.

VITAMIN-RESISTANT RICKETS. A. MORTON GILL, Arch. Dis. Childhood **14**:50 (March) 1939.

Four cases of rickets are described, in none of which was there any evidence of malnutrition, lack of sunlight, calcium drain, celiac disease or renal disease and in none of which did any of the known forms of therapy, given over a period of several years, produce evidence of healing. Healing occurs spontaneously when growth ceases. It is suggested that the fault may be a failure of utilization at the site of osseous growth. KELLY, Milwaukee.

SCURVY IN IDENTICAL TWINS. A. LINOSSIER-ARDOIN and D. RONGET, Bull. Soc. pédiat. de Paris **37**:40 (Jan.) 1939.

Identical twins, boys 2 years old, had scurvy. Despite negative serologic reactions they were thought to have congenital syphilis. The scurvy was treated with a diet rich in vitamin C in one and with injections of ascorbic acid in the other. The latter patient improved much sooner than the former.

BENJAMIN, Montreal, Canada.

ANTIRACHITIC VITAMINS D_2, D_3 AND D_4 AND THEIR USE IN LARGE DOSES FOR THE TREATMENT AND PROPHYLAXIS OF RICKETS AND SPASMOPHILIA. I. GATTO, Lattante **10**:26 (Jan.) 1939.

This article is a review of the recent literature on sterols and vitamin D.

HIGGINS, Boston.

VITAMIN B_1 AND SERUM LIPASE. P. CORUZZI, Lattante **10**:63 (Feb.) 1939.

The ability of the blood serums of 8 children with various diseases to split tributyrin was studied before and after two weeks of the daily parenteral injection of 500 international units of vitamin B_1. There was an increased splitting of the fat after the vitamin therapy; this indicated either an increased amount or increased function of the serum lipase. An exception occurred in 1 child with an eczematous diathesis. HIGGINS, Boston.

BARLOW'S DISEASE (SCURVY). EVELINA MONTANARI, Lattante **10**:109 (March) 1939.

Four cases of scurvy, 2 with necropsy, are reported. HIGGINS, Boston.

METABOLISM OF VITAMINS IN NURSLINGS. V. BAPTISTA, Pediatria prat. **9**:307 (July-Aug.) 1938.

The author reviews the importance of the various vitamins in pregnancy but states that even rather marked deficiencies in maternal diet are not reflected in

the fetus, because the placenta actively consigns available vitamins to the fetus at the expense of the mother. After birth the mother continues to supply vitamins to the infant through the breast milk. Included is a table from Neuwieler's book which shows that mother's milk has more of vitamins A and C and less of vitamin B than cow's milk. The vitamin requirements of infants are discussed.

DIETRICH, Beverly Hills, Calif.

SYMPTOM COMPLEX AND ETIOLOGY OF MOELLER-BARLOW'S DISEASE. C. BENNHOLDT-THOMSEN, Med. Klin. **35**:136 (Feb. 3) 1939.

After describing the typical pathologic picture of scurvy and its relation to avitaminosis C, the author discusses latent scurvy, which may be manifested by petechiae, hematuria, blood-streaked nasal secretion, flecks of bloody mucus in the stool, stationary weight, pallor, weakness and decreased resistance. Attention is called to Rietschel's work, according to which the vitamin C requirement is probably much lower than that generally indicated in the literature.

SIEMSEN, Chicago.

OCCURRENCE OF VITAMIN C IN THE PLACENTA. W. NEUWEILER, Ztschr. f. Geburtsh. u. Gynäk. **118**:27 (Nov.) 1938.

Histochemical examination of placentas showed that the vitamin C content is greatest in the syncytium but that the vitamin is also present in the stroma and in the decidua. On chemical examination the author found a considerable amount of vitamin C in the decidua but not as much as in the placenta, the concentration depending on the intake of vitamin C by the mother. According to the author, both the decidual and the placenta are depots of vitamin C, the former especially during the first half and the latter especially during the second half of pregnancy.

ADAIR and POTTER, Chicago.

ABSORPTION OF SMALL AMOUNTS OF FAT FROM THE INFANT'S INTESTINE: AN INVESTIGATION REGARDING THE BASIS OF TREATMENT WITH MASSIVE DOSES OF IRRADIATED ERGOSTEROL (VIGANTOL). F. KÜSTER, Ztschr. f. Kinderh. **60**: 458 (Dec. 19) 1938.

Küster observed that a massive dose of irradiated ergosterol (vigantol) frequently failed to cure rickets when given without a meal at a welfare clinic. Since most reports regarding the favorable effect of a massive dose of vigantol have emanated from clinics or hospitals where the oil is given in combination with food, the author decided that in his cases faulty absorption was probably responsible for the failures. Studies of absorption were made by giving infants iodized oil: (1) plain oil, (2) emulsified oil, (3) plain oil with food and (4) emulsified oil with food. The results with plain oil corresponded quite closely with the clinical failures with vigantol. The absorption with emulsified oil was good. The combination with food increased the absorption of plain oil but had little enhancing effect on the absorption of emulsified oil.

SIEMSEN, Chicago.

LATE RICKETS CURED BY A MASSIVE DOSE OF VITAMIN D_3. A. NADRAI, Ztschr. f. Kinderh. **60**:590 (Feb. 18) 1939.

Although infantile rickets is primarily a vitamin deficiency disease, rachitis tarda may be secondary to other disorders, renal, hepatic or intestinal. The author reports the case of a child 4½ years old who, after having had a severe prolonged intestinal disorder (dysentery?) at 1½ years, had florid rickets which did not respond to ordinary vitamin D therapy. Complete cure followed intramuscular administration of a single large dose (25 mg.) of vitamin D_3.

SIEMSEN, Chicago.

AVITAMINOSIS A. PAUL LUKI, Časop. lék. česk. **76**:399 (April 2) 1937.

The author makes a short summary of the literature on avitaminosis and discusses the dietary control, the pathogenesis and the symptoms of the condition. In the case presented there was polyavitaminosis (A, B and D). The chief symptoms were day blindness, xerophthalmia, polyneuritis and tetany.

STULIK, Chicago.

ASCORBIC ACID CONTENT OF THE BLOOD OF MOTHER AND FETUS. C. WAHREN, Nord. med. tidskr. **15**:193 (Jan. 29) 1938.

The method of Lund and Lieck was used. The blood of 17 mothers and that from the umbilical vein of their newborn babies was examined (December). In the mother the ascorbic acid content showed variations from 0.04 to 0.28 (average 0.16) mg. per hundred cubic centimeters, and that of the umbilical venous blood from 0.12 to 0.48 (average 0.35) mg.

WALLGREN, Göteborg, Sweden.

INFLUENCE OF VITAMIN A ON THE EXTERNAL SECRETION OF THE PANCREAS. KAREL HERFORT, Acta med. Scandinav. **96**:425 (Oct. 21) 1938.

The author compared the effect on the external secretion of the pancreas of the intravenously injected secretin with that of the administration of vitamin A (20,000 international units) by duodenal tube or by intramuscular injection in 80 patients.

Twenty of these had pancreatic lesions verified by operation; 40 had probable but not proved pancreatic lesions, and 20 had no evidence of gastrointestinal (or pancreatic) disease.

In all patients the vitamin A seemed to be the more effective stimulus for the pancreatic secretion, as was evidenced both by the increased amount of duodenal juice obtained and by the increased trypsin and lipase activity.

KAJDI, Baltimore.

Hygiene; Growth and Nutrition; Public Health

CONTROLLABLE ELEMENTS IN INFANT MORTALITY. F. A. KASSEBOHM and M. J. SCHREIBER, New York State J. Med. **38**:1165 (Sept. 1) 1938.

A study was made of 3,188 obstetric deliveries at the Lutheran Hospital of Manhattan during a ten year period. Children under 1,500 Gm. in weight were not included. There were 182 infant deaths, which are studied under different diagnostic heads. Of 25 deaths reported as due to operative trauma, 17 occurred after forceps had failed and version had immediately been attempted. The authors feel that this is a serious error and that a reasonable interval of time should elapse between the two operative procedures. Such a pause permits readjustment of the fetus and gives an opportunity to deepen the anesthetic state.

Prematurity, prolonged labor and other factors are also discussed.

The importance of better and more frequent necropsies is stressed. "There is room for reduction in infant mortality by the exercise of obstetric judgment and skill."

AIKMAN, Rochester, N. Y.

MORTALITY OF CHILDREN IN ENGLAND AND WALES AND GERMANY: A STATISTICAL COMPARISON. G. TUGENDREICH, Brit. M. J. **1**:918 (May 6) 1939.

This article is entirely statistical and does not lend itself to abstracting.

ROYSTER, University, Va.

THIRTY YEARS OF A WELL BABY CLINIC. R. S. CUIZZA, Lattante **10**:157 (April); 209 (May) 1939.

Statistics have been assembled from the records of the Consultorio per Lattanti of the Maria Vittoria Hospital in Turin, Italy, during its first thirty years, from

1907 to 1937. During this time 8,431 infants paid 91,022 visits to the clinic. During the last ten years the visits totaled 50 per cent more than those of the previous twenty years. Of these infants, 75 per cent were wholly breast fed and 13 per cent partly breast fed during the first two months of life; during the fourth and fifth months of life 48 per cent were wholly breast fed and 21 per cent partly breast fed. The babies on breast feedings averaged approximately 1 to 2 pounds (0.5 to 1 Kg.) heavier during the first two years of life than the bottle-fed infants. The percentage of nursing mothers was approximately the same in all years of the period, although in the later years more of the babies received complementary feedings in addition to the breast milk; the infants of the earlier years of the period usually showed better gain in weight. Only 20 per cent of the mothers of twins were able to nurse both babies.

HIGGINS, Boston.

Prematurity and Congenital Deformities

INJURY OF THE CHILD BY ROENTGEN RAY DURING PREGNANCY: REPORT OF A CASE. F. ELMER JOHNSON, J. Pediat. **13**:894 (Dec.) 1938.

A case of cerebral anomaly following exposure to roentgen rays in utero is reported. The patient was a 6½ month old feeble marasmic infant with hydrocephalus, spasticity of all four extremities and microphthalmia. He died from purulent meningitis following puncture of the fontanel. Autopsy revealed: agenesis of the frontal cerebral hemispheres; maldevelopment of the third ventricle, the geniculate bodies, the optic thalamus, the optic tracts, the corpus callosum and the fornix; absence of the aqueduct of Sylvius; microphthalmos; external hydrocephalus; purulent meningitis, and bronchopneumonia. The mother had been given three roentgen treatments for fibroids of the uterus, receiving a total of 400 roentgen units over a period of fifteen days. It was estimated that the three treatments given were on approximately the seventeenth, the twenty-fourth and the thirty-second day after conception. A review of the literature reveals the accumulated evidence of danger to the fetus from irradiation of a pregnant woman. Either abortion will result, or (in over 50 per cent of live births) there will be gross defects of the central nervous system and of the eyes. The high percentage of lesions of the central nervous system and of the eyes and the astonishing relative absence of other anatomic defects suggest that sensitivity of fetal nervous tissue to roentgen ray and radium is most important. The chance of injury is proportional to the size of the dose and the nearness of the treatment to conception, for the eyeballs of the early fetus are relatively larger and less protected than they later become. Possible intercurrent infections and individual radiosensitivity are also factors. Early fetal neural and optic tissues are highly susceptible to the roentgen rays. Irradiation of the mother in regions remote from the uterus may also be harmful to the fetus.

RAUH, Cincinnati.

CONGENITAL DEFORMITIES OF LEGS. R. BROOMHEAD, Brit. M. J. **2**:1311 (Dec. 24) 1938.

Broomhead reports a very interesting bilateral deformity and describes the orthopedic apparatus applied, which enabled the patient to walk in a fairly normal manner.

ROYSTER, University, Va.

DOLICHOSTENOMELIA (MARFAN'S DISEASE). PAUL GIRAUD, BOCCA, JAYLE and MOCKERS, Bull. Soc. pédiat. de Paris **36**:713 (Nov.) 1938.

A girl 9 months old had long extremities, ocular abnormalities and a slight cardiac anomaly. She was thought to have dolichostenomelia. This condition is accompanied by hypersusceptibility to infection. The infant died of bronchopneumonia.

BENJAMIN, Montreal, Canada.

THORACOSCHISIS IN A SEVEN AND ONE-HALF MONTH FETUS. GEORGE ILBERG, Ztschr. f. Geburtsh. u. Gynäk. **117**:492 (Sept.) 1938.

The author gives a detailed description of a case of this malformation. The anomalies present were: arrest of development of the ribs of the right side (thoracoschisis); scoliosis of the thoracic portion of the spine; displacement of the diaphragm toward the right and upward; eventration of abdominal organs under the skin of the chest on the right side; aplasia of the right lung, of the uterus and adnexae on the right and of the pancreas; atresia of the anus; absence of almost the entire large intestinal tract; intestinovaginal and vesicovaginal fistulas; absence of the urethra; horseshoe kidney; fusion of the adrenal glands; a cleft hand with six fingers, and absence of one umbilical artery.

Of these malformations thoracoschisis and fusion of the adrenals are the rarest.

ADAIR and POTTER, Chicago.

"PHENYLPYRUVIC OLIGOPHRENIA." E. GORTER and J. THERON, Maandschr. v. kindergeneesk. **8**:329 (May) 1939.

The article is a general survey of the symptoms, the heredity and the peculiarity of the metabolism of children suffering from mental deficiency associated with excretion of phenylpyruvic acid (phenylpyruvic oligophrenia). The oligophrenia has been described and studied by Fölling (1934), Jervis (1937) and Penrose and Quastel (1935, 1937).

VAN CREVELD, Amsterdam, Netherlands.

Newborn

CLINICAL STUDIES OF INSTINCTIVE REACTIONS IN NEW BORN BABIES. MARGARETHE A. RIBBLE, Am. J. Psychiat. **95**:149 (July) 1938.

After a study of many infants from birth to several months of age the author postulates that cortical behavior is closely linked with physical equipment. The greater the size of the baby at birth, the higher the mental activity. Infants who have ample breathing and sucking activity rapidly attain a good organization for breathing and eating functions. They are then hungry for tactile experiences and hence have a desire to explore their environment.

JAHR, Omaha.

MELENA OF THE NEWBORN CURED BY TRANSFUSION. M. CAMNER, Bull. Soc. de pédiat. de Iasi **9**:38, 1938.

A case is reported.

LESLIE, Evanston, Ill.

SYPHILITIC CHANCRE IN A NEWBORN INFANT ACQUIRED DURING DELIVERY. G. NASTASE, Bull. Soc. de pédiat. de Iasi **9**:40, 1938.

A chancre developed on the scalp of an infant during the third week of extrauterine life. Secondary lesions of the skin and mucous membranes were present when the child was 2 months of age. The mother was suffering from secondary lesions at the same time; she stated that these had been present for thirty days. The mother had been infected during the eighth month of pregnancy. The placenta must have been an effective barrier to the transmission of infection during intrauterine life.

LESLIE, Evanston, Ill.

FAMILIAL ICTERUS GRAVIS OF THE NEWBORN WITHOUT ERYTHROBLASTOSIS. A. ARONDEL, Bull. Soc. pédiat. de Paris **36**:670 (Nov.) 1938.

A newborn boy showed marked jaundice during the first day of life. This persisted for several days, and he became pale, weak and hypertonic. A blood smear showed slight anemia but no increase of erythroblasts. He was given repeated injections of maternal blood and hepatic extract. He recovered but

showed evidence of retarded development at 9 months and again at 18 months of age. Three infants born previously to the same mother all died during the early days of life, apparently from a similar condition.

BENJAMIN, Montreal, Canada.

SYMMETRIC GANGRENE OF THE EXTREMITIES IN A NEWBORN INFANT. PIERRE BARBÉ, Bull. Soc. pédiat. de Paris **37**:45 (Jan.) 1939.

A boy who did not thrive and had diarrhea and vomiting showed gangrene of several fingers a few days after birth. This progressed and involved the hands and areas about the knees. He died on the twentieth day after birth.

BENJAMIN, Montreal, Canada.

NUMBER AND FRAGILITY OF RED CELLS IN THE FIRST DAY OF LIFE, WITH PARTICULAR REGARD TO ICTERUS NEONATORUM. U. GALLERANI, Lattante **9**:488 (Nov.); 529 (Dec.) 1938.

During the first twenty-four hours of life the red blood cell count increased in the cases of 10 of 13 infants without jaundice and decreased in the cases of 10 of 13 infants with jaundice. The fragility of the red cells was essentially the same for infants with and for those without jaundice. Seventeen per cent of the red cells were hemolyzed in a 0.7 to 0.6 per cent saline solution, 68 per cent in a 0.5 to 0.4 per cent saline solution and 12 per cent in a 0.3 to 0.2 per cent saline solution. In icterus neonatorum, therefore, there is destruction of red cells, but this destruction is due to physical conditions and not to increased fragility of the cells.

HIGGINS, Boston.

PAROXYSMAL TACHYCARDIA IN A NEWBORN CHILD. A. PUGLISI, Arch. argent. de pediat. **11**:3 (Jan.) 1939.

The author reports a case of this condition in an infant 10 days old. The pulse rate reached 345 per minute. The child showed a congenital cardiac malformation. Electrocardiograms indicated that the pathologic condition was probably in the sinoauricular node and related to the anatomic fault.

SCHLUTZ, Chicago.

EDEMA OF THE NEWBORN. H. VOLZ, Ztschr. f. Geburtsh. u. Gynäk. **117**:131 (April) 1938.

A classification of the different forms of generalized and localized edema of the newborn is given. The author's case of congenital lymphangiectatic edema is similar to 12 others reported in the literature. The condition most frequently involves the extremities, is always a pitting edema and is tense at first and softer later. Other parts of the skin are very loose. Therapy has been without result in all cases, although some spontaneous improvement may occur with increasing age.

ADAIR and POTTER, Chicago.

THE NATURE OF THE ORAL ZONE OF THE NEWBORN. K. EISSLER, Ztschr. f. Kinderpsychiat. **5**:81 (Sept.) 1938.

This article includes a description of the movements of the various muscles concerned with nursing. The psychologic factors are discussed. Tracings are presented to portray the various curves expressed in the process of suckling by the infant, in response to different stimuli to the buccal surfaces.

JAHR, Omaha.

STUDIES ON SECRETION OF SWEAT IN THE NEWBORN. SHIGESHI UCHINO, Jap. J. Obst. & Gynec. **20**:9 (Jan.) 1939.

Twenty-eight of 57 full term infants first showed evidence of secretion of sweat from two to eighteen days after birth. In 15 per cent of the 28 secretion occurred between the third and the fifth day. In 4 infants born between the thirty-fourth

and the thirty-seventh week of pregnancy sweat first appeared from thirteen to twenty-four days after birth. One showed no evidence of secretion thirty-three days after birth.

Pilocarpine injected into the skin of infants born as early as the twenty-eighth week of gestation gives local secretion of sweat. Absence of the secretion after birth is due to immaturity of the center controlling secretion and not to inability of the glands to secrete.

ADAIR and POTTER, Chicago.

VOMITING OF NEWBORN INFANTS. T. HALBERTSMA, Maandschr. v. kindergeneesk. **8**:295 (May) 1939.

Six cases of persistent vomiting of the newborn are described. In 3 cases the cause was esophageal atresia; in 2, duodenal stenosis. In the sixth case there was occlusion of the stomach by pyloric aplasia.

VAN CREVELD, Amsterdam, Netherlands.

Acute Contagious Diseases

THE NEUROLOGICAL COMPLICATIONS OF WHOOPING COUGH: A REVIEW OF THE LITERATURE WITH THE REPORTS OF TWO CASES OF PERTUSSIS ENCEPHALITIS. RICHARD L. NELSON, J. Pediat. **14**:39 (Jan.) 1939.

The neurologic complications of pertussis have received scant attention in the pediatric literature. Nelson reviews the literature and discusses the etiology and symptomatology of these complications. The most likely explanation for the occurrence of neurologic phenomena during pertussis are: (1) intracranial hemorrhage, which occurs rarely, (2) spasmophilia, which accounts for convulsions in some cases but which can hardly be thought to explain the more severe disturbances; (3) functional vascular lesions resulting in stasis or prestasis, and (4) encephalitis, either hemorrhagic or nonhemorrhagic, which from available autopsy studies seems to be present in a large percentage of the cases. The nervous complications of pertussis make their appearance either at the peak of the paroxysmal stage or after it has begun to subside. The onset may be either sudden or insidious. Young children are more prone to suffer neurologic complications, though such complications may occur at any time during childhood. The most common manifestation of neurologic involvement is the convulsion. The convulsion is nearly always clonic, and frequent recurrence is common. Coma and paralysis follow the convulsion in some instances. Sensory disturbances are rare. Blindness, both temporary and permanent, and deafness have been observed. Psychic disturbances, such as disturbances of sleep, amnesia, anxiety, neuroses and mental depression, are common. Coma, delirium and melancholia may occur without preceding convulsions. As late results of the neurologic disturbances of pertussis epilepsy, mental retardation, spastic paralysis or other disturbances may occur. Nelson concludes his report with an abstract of 2 cases of pertussis encephalitis with complete recovery.

RAUH, Cincinnati.

THE SERUM TREATMENT OF MENINGOCOCCIC MENINGITIS. CHARLES J. LESLIE and ADOLPH G. DE SANCTIS, J. Pediat. **14**:83 (Jan.) 1939.

This paper is based on a study of 75 cases of meningococcus meningitis treated with antibacterial serum. The results obtained are compared with those obtained with other remedies, notably antitoxin alone and sulfanilamide. Antibacterial serum was administered intrathecally once in twenty-four hours (rarely twice in twenty-four hours). Intravenous injections of the serum were given only in the presence of severe toxicity, rash and fever indicating bacteremia. Serum was given intramuscularly only when intravenous injection was not possible. The mortality rate for these 75 cases was 15 deaths (20 per cent). The

authors conclude that meningococcic infections can be treated effectively with antibacterial serum; that intraspinal administration of serum is essential except in case of bacteremia without meningeal involvement, and that the conservative method of therapy as discussed in this paper is the method of choice.

RAUH, Cincinnati.

DIPHTHERIA. C. H. MAXWELL, B. L. CULLEN and R. J. THOMAS, New York State J. Med. **38**:1227 (Sept. 15) 1938.

For years Auburn, N. Y., had had an excellent record in the high percentage of children immunized against diphtheria and the very low incidence of the disease. However, in the late fall of 1935, within one month 3 diphtheritic children and a carrier were found in one section of the city. There was fear of an outbreak of the disease, and many nose and throat cultures were taken. A study of these cultures and of previous records show that throat cultures positive for diphtheria are exceedingly rare in a well immunized community. In 1934 over 500 throat cultures were taken in Auburn without finding a single positive culture. Repeated Schick tests are essential for effective protection of a community.

AIKMAN, Rochester, N. Y.

PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **54**:969 (June 9) 1939.

In the period of April 23 to May 20, 1939, the incidence of poliomyelitis was 2.3 times greater than it was during the same period in 1938, owing to an increase in South Carolina, Georgia and Florida. Influenza was declining, but was still above the seasonal level (4 times). Smallpox was still above the seasonal level, particularly in the Central States. Diphtheria, measles, meningitis, typhoid and scarlet fever were below the seasonal levels. The mortality from all causes was 11.3 per thousand, which is slightly below the average rate for the last five years.

SANFORD, Chicago.

ACUTE ANTERIOR POLIOMYELITIS: FOUR SIMULTANEOUS CASES IN A SCHOOL. G. O. BARBER, Brit. M. J. **2**:1137 (Dec. 3) 1938.

Acute anterior poliomyelitis appeared simultaneously in 4 boys in a boarding school. An inquiry was made into the manner of their infection, and the evidence suggests a route which may be worthy of experimental investigation. After studying the outbreak along several lines, Barber narrows the investigation down to a possible gastrointestinal origin quite analogous to food poisoning, on the grounds that:

1. The seasonal and climatic incidence (see accompanying graphs from the New York Health Bureau) agrees closely with the seasonal increase in the consumption of fresh garden produce and its climatic maximum production.

2. The epidemiologic distribution of the disease does not resemble that of infections of the respiratory tracts; it resembles that of food poisoning and typhoid.

3. The disease is definitely *not* highly infectious. Until recently, patients with this disease were nursed from the start in the general wards of general hospitals, and there have been no well authenticated cases of infection transmitted to contacts. In this recent outbreak certain of the patients were members of crowded families, and their illness was not reported until it had been in the paralytic stage for several days. During this time other children had been sleeping every night in the same beds as the paralyzed children, and in no case was one of these contacts affected later.

4. The virus, according to some investigators, is recoverable from the feces of patients, proving that it is present in the alimentary canal.

5. In the classic case recorded by Draper a carrier was definitely postulated from the evidence as being a Greek fruiterer. All the patients had been in con-

tact with him as business associates, relations or customers, and there is nothing in the evidence to indicate that the man was a carrier or that the infection was spread other than by the fruit he supplied.

A line of investigation is suggested here to workers on this virus.

ROYSTER, University, Va.

TREATMENT OF DIPHTHERIA WITH REFINED ANTITOXIN. A. HUTCHISON, Brit. M. J. **1**:384 (Feb. 25) 1939.

Hutchison reports on a refined diphtheria antitoxin manufactured by Burroughs Wellcome Company through Pope Company. Among 200 patients treated with this antitoxin the death rate was only 2.5 per cent. No serum rashes were recorded, and immediate reactions after intravenous injections were few. The small bulk of the serum caused the patient less discomfort than the ordinary concentrated serum.

The percental incidence of gravis diphtheria in the Glasgow area seems to be on the upgrade.

Chewing gum appears to be useful in adenitis, apparently causing massage of the cervical glands by the action of the jaw in chewing.

ROYSTER, University, Va.

SULPHANILAMIDE IN THE TREATMENT OF MEASLES. T. ANDERSON, Brit. M. J. **1**:716 (April 8) 1939.

In a small series of patients with measles Anderson used sulfanilamide on alternate patients in an effort to prove or disprove that this drug is of value in the prevention of the commoner complications of measles. He feels that when bronchopneumonia occurred, the duration was shortened to some extent and that there was a possible prevention of otitis media. In other respects his report is noncommittal.

ROYSTER, University, Va.

ACUTE MENINGOCOCCIC INFLAMMATION OF THE ADRENALS (WATERHOUSE-FRIDERICHSEN SYNDROME). E. RUTISHAUSER and H. BARBEY, Ann. d'anat. path. **13**:143, 1936.

The article presents a review of the literature on adrenal hemorrhage. A case is presented, in which the background was meningococcic septicemia. There were complex clinical and anatomic findings, including multiple areas of myositis in the pharyngeal muscles, tongue and diaphragm; acute myocarditis; hyperemia of the islands of Langerhans and of the mucosa of the trachea and bronchi; thrombosis and necrosis of the glomerular tufts of the kidney; diffuse hepatitis and thrombosis of the central veins; necrosis of the pulmonary elastic tissue, and other changes, as well as other septic findings. There was also bilateral adrenal hemorrhage with thrombosis of the veins. In a somewhat philosophic discussion of the physiologic mechanisms involved, an attempt is made to separate the endocrine from the septic factors.

PERRY J. MELNICK. [ARCH. PATH.]

INFECTIOUS JAUNDICE WITH PNEUMOCOCCEMIA FOLLOWING MEASLES. P. LEREBOULLET, M. LELONG, ROUDINESCO and JEAN BERNARD, Bull. Soc. pédiat. de Paris **36**:460 (July) 1938.

A boy 7 years old was recovering from measles. He had pleuropneumonia at the base of the right lung and obstructive jaundice. Culture of the blood as well as of fluid aspirated from the right hemithorax yielded growths of pneumococci of type V. The boy recovered. It is pointed out that jaundice occurs not infrequently as a complication of pneumococcemia.

BENJAMIN, Montreal, Canada.

TWO CASES OF BILATERAL PLEURISY FOLLOWING MEASLES. RITA SHELTON-ARNOLDSON, Bull Soc. pédiat. de Paris **36**:665 (Nov.) 1938.

A boy 23 months old and a girl 26 months old showed physical signs and roentgen evidence of pleurisy following measles. In both cases the condition cleared up entirely. Repeated tuberculin tests gave negative results, and guinea-pigs inoculated with the gastric contents failed to show any evidence of tuberculosis.

BENJAMIN, Montreal, Canada.

PSYCHOTIC FORM OF EPIDEMIC PAROTITIS. C. I. URECHIA, Encéphale **2**:144, 1938.

Only 12 cases of epidemic parotitis with necropsy have been reported. In only 4 of these was the brain examined microscopically. The lesions consisted of hemorrhage, congestion, mild perivascular infiltration with lymphocytes, patchy demyelination, formation of glial nodules and meningitis. These lesions were not all present in each case. In 1 case only congestion of the parenchyma and slight meningeal infiltration were shown. The present report concerns a woman aged 54 who suffered from acute confusion and mania, with logorrhea, agitation, flight of ideas, incoherence, unsystematized ideas of persecution, anxiety and anorexia. This state lasted for five days before the appearance of bilateral parotitis. The pulse rate was 120. There was no fever. The patient died with signs of heart failure seven days after onset of the mental symptoms and seven days after onset of the parotitis. The brain was congested and edematous. Along the fissures were streaks of meningitic involvement. Microscopically there were patches of discrete infiltration with lymphocytes and plasma cells, and small hemorrhages in the meninges. The cerebral cortex presented discrete cellular lesions of the acute type of Nissl, chiefly in the superficial three layers. There was no degeneration of myelin or axons. The ganglion and glia cells contained abundant fat. In 2 other cases of mumps there was also psychosis at onset and death was associated with myocarditis.

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

MENINGITIS ASSOCIATED WITH MUMPS. G. DE MATTOS and J. WOISKI, Pediatria prat. **9**:321 (July-Aug.) 1938.

The authors review the subject of meningitis associated with mumps and stress the fact that the meningeal symptoms may appear before, during or after swelling of the parotid glands. Three cases are reported. The authors feel that the prognosis as to both life and intact mentality is good.

DIETRICH, Beverly Hills, Calif.

A CASE OF MEASLES IN WHICH GIANT CELLS WERE OBSERVED IN THE RESPIRATORY TRACT. M. MASUGI and G. MINAMI, Beitr. z. path. Anat. u. z. allg. Path. **101**:283, 1938.

Masugi and Minami report their pathologic observations on a 9 month old girl who died of secondary bronchopneumonia four days after the appearance of a measles exanthem. The buccal, faucial, pharyngeal, bronchial and esophageal mucous membranes revealed many multinucleated giant cells containing inclusion bodies. None was noted in the tonsils, appendix, mesenteric lymph nodes and spleen. In morphologic structure the giant cells, which are regarded as having their origin in local epithelial cells, corresponded completely to those described by Warthin and Finkeldey, as occurring in tonsils removed during the prodromal stage of measles. They contained many crowded hyperchromatic nuclei. Regressive changes in both the nuclei and the cytoplasm may be present. The inclusion bodies are usually multiple and are situated close to the nuclei. The inclusion bodies vary considerably in size and are round in contour in their typical form. They are counterstained a homogeneous intense red color in hematoxylin and eosin preparations. Measles is regarded as a disease caused by an epitheliotropic virus.

R. J. LEBOWICH. [ARCH. PATH.]

PREPARALYTIC STAGE OF INFANTILE PARALYSIS. O. KAUDERS, Med. Klin. **34**:1182 (Sept. 9) 1938.

The symptoms from the upper respiratory tract in the preparalytic stage of poliomyelitis are usually mild. Signs of meningeal irritation, which are practically always present, are of diagnostic importance. The position of the patient is quite characteristic, the lying on his side, with the legs flexed. The "spine sign," first described by Americans, consists of a sudden and painful contraction of the neck muscles when the head, grasped by the examiner's hands, is thrust forward so that the chin approaches the chest. The extremities are sensitive to pressure and may be painful or hyperesthetic. There may be ataxia or uncertainty of motion, with trembling. The reflexes are diminished or absent. Kernig's sign is usually present. The examination of the spinal fluid is important. Kauders urges great care in detecting this disease in the preparalytic stage, so that convalescent serum may be given earlier enough to prevent paralysis. SIEMSEN, Chicago.

COURSE OF DIPHTHERIA DURING THE YEARS 1934-1936. M. VAGADES, Med. Klin. **34**:1189 (Sept. 9) 1938.

Vagades discusses various phases of an epidemic of diphtheria which occurred in Witten-Ruhr, Germany. Active immunization of 13,700 preschool and school children was carried out during the epidemic. The morbidity ratio of immunized to nonimmunized preschool children was 1.8:4.0; the ratio among school children was 0.9:9.1. The mortality ratio of immunized to nonimmunized children was 1:22. The effect of immunization on the course of the epidemic cannot be evaluated so accurately. Vagades seems conservative. Some German authors are still skeptical regarding the value of active immunization. SIEMSEN, Chicago.

QUESTION COMPLEX OF DIPHTHERIA. F. V. BORMANN, Med. Klin. **34**:1419 (Oct. 28) 1938.

The carrier is the most common source of infection. A large proportion of children are carriers at one time or another. Single cultures are of practically no value because of the variability in cultures made on different days. Segregation of all children in whose cases cultures yield bacteria is impractical; only those convalescing from diphtheria or those who have been in contact with the disease need be isolated. Furthermore, it would be undesirable because the presence of the bacillus in the nose and throat probably plays an important role in the acquisition of natural immunity.

Active immunization is desirable under certain circumstances, but general immunization is undesirable, in Bormann's opinion, because it interferes with natural acquisition of immunity via silent infection. Persons not acquiring natural immunity will probably not be permanently protected by artificial immunization. Finally, artificial immunity is only antitoxic, not antibacterial. With serum treatment the mortality of diphtheria is not very high. SIEMSEN, Chicago.

DESTRUCTION OF FUNCTION OF THE INTERNAL EAR IN SCARLATINAL OTITIS. E. URBANTSCHITSCH, Monatschr. f. Ohrenh. **73**:1 (Jan.) 1939.

The loss of function of the internal ear in cases of scarlet fever is usually produced by serous labyrinthitis, even when there is severe suppuration in the pneumatic cells around the internal ear. When the condition is mild repair of the function of the internal ear may be expected even when the patient is entirely deaf. In a large majority of cases of severe involvement, however, the normal function of the internal ear will not return. Particularly is this true when the patient has acute otitis media prior to the appearance of the exanthem and when

otitis occurs soon after the appearance of the exanthem and the patient is in danger so far as the labyrinthitis is concerned. The fact that in scarlatinal otitis labyrinthitis is usually serous and seldom becomes purulent may be explained by the development of the scarlatinal antivirus within the body, producing greater resistance against the local suppuration. The author presents 4 cases, and three photomicrographs accompany the article.

LEDERER, Chicago. [ARCH. OTOLARYNG.]

AGGLUTINATION OF PERTUSSIS BACILLI AS AN EARLY DIAGNOSTIC SIGN IN INFANCY. C. BENNHOLDT-THOMSEN and W. DIEUST, Ztschr. f. Kinderh. **60**:445 (Dec. 19) 1938.

Using the technic (described in detail) of Hansen, who published a paper, "Agglutinin Formation in Pertussis," in the current volume of this journal, the authors examined 150 infants and children. For comparison, they performed the complement fixation reaction also. The agglutination reaction was found to be positive much earlier (during the catarrhal stage) and much more consistently positive during early infancy. Agglutinins are formed even during the first three months of life, at which time complement-binding antibodies are not formed. When pneumonia complicates pertussis, the agglutination reaction becomes negative, to become positive again after recovery from the pneumonia. The agglutination reaction makes possible a relatively early diagnosis.

SIEMSEN, Chicago.

BLOOD SUGAR LEVEL IN DIPHTHERIA. GEORGIANA PISAROVIC-CIZEK, Časop. lék. česk. **76**:493 (April 23) 1937.

A short review of the literature is followed by a study of 80 children between 3 and 14 years of age. "Fasting blood" was tested according to the method of McLean. The sugar level is no criterion of the severity of the infection. During the first week the average value for sugar was about 200 mg. per hundred cubic centimeters of blood; during the second and third weeks it was always over 100 mg. and sometimes over 200 mg. During the fourth, fifth and sixth weeks it was about 200 mg. and only occasionally fell to 110 mg. Forty cubic centimeters of 40 per cent dextrose with insulin had a favorable result in cases of mild involvement in spite of a rapid fall in the value for blood sugar, while in the cases of severe involvement there was rapid development of hypoglycemia (in thirty minutes), with collapse. The injury to the adrenals by the toxin induces instability in the insulin and sugar equilibrium, and the repeated "dextrose venoclysis" is regarded as excellent therapy. This is true especially in cases of myocardial involvement, in which direct increase in cardiac muscle tonus is obtained in addition to the general nutrition, tissue repair and improvement in mental attitude.

STULIK, Chicago.

MASTIC REACTION IN CASES OF ACUTE ANTERIOR POLIOMYELITIS. K. G. KAIJSER, Acta med. Scandinav. **98**:209 (Jan. 12) 1939.

Kaijser says that little attention has been given to the mastic reaction in cases of acute anterior poliomyelitis. Nevertheless, several observers have shown that a type of mastic reaction can be evolved which is characteristic for poliomyelitis. The mastic test has been employed for the demonstration of experimental poliomyelitis in monkeys as well as for the early diagnosis of poliomyelitis in human subjects. Kaijser studied the value of the test first in 14 cases of acute anterior poliomyelitis accompanied by paralysis. He reports the clinical histories in these cases and the results of the mastic test. It was found that in certain cases of poliomyelitis in which paralysis exists at the time of the examination of the cerebrospinal fluid there is a typical mastic reaction. In the majority of these cases

only moderate flocculation was observed in the tube that contained the strongest concentration, and the maximum of flocculation appeared in the second, third and fourth tubes. In the succeeding tubes it subsided; it usually disappeared completely in the sixth or seventh tube. The average curve of the mastic reaction in these cases is represented by the figures 123321000. Having determined that in poliomyelitis with paralysis there is a typical curve, the author studied the mastic reaction in cases of two other types of disorders, namely, in 10 cases of acute anterior poliomyelitis without paralysis and in 5 cases in which poliomyelitis was suspected. In the 10 cases of abortive poliomyelitis the curve of the mastic reaction was not as uniform or as characteristic as in the cases of poliomyelitis that was accompanied by paralysis. In the cases of the abortive type the maximum flocculation was usually observed in tubes 2, 3 and 4. In the 5 cases in which poliomyelitis was only suspected, the mastic reaction was similar to that under normal conditions. The impression was gained that in these 5 cases there existed a disorder other than poliomyelitis.

J. A. M. A.

ENCEPHALITIS AFTER GERMAN MEASLES. LARS HALLÉN, Nord. med. tidskr. **15**:54 (Jan. 8) 1938.

The author reports the cases of 1 girl and 2 boys, respectively 15, 13 and 13 years of age, who fell ill on the fifth, fourth and second day after the eruption of German measles with convulsions, fever, unconsciousness and pleocytosis. Complete recovery occurred.

WALLGREN, Göteborg, Sweden.

POLIOMYELITIS IN INFANTS. ROLF BERGMAN, Nord. med. tidskr. **15**:1000 (June 18) 1938.

The author reports briefly 9 cases of poliomyelitis in children under 1 year of age. The youngest child was 7 weeks old. In all cases but 1 there had been other patients with poliomyelitis in the environment. Four of the children were under 6 months of age. Of these, 1 had received only breast milk; the other 3 had had complementary feedings with boiled cow's milk mixtures.

WALLGREN, Göteborg, Sweden.

PROLONGED MENINGOCOCCUS MENINGITIS SUCCESSFULLY TREATED BY DRAINAGE. HANS JENSENIUS, Nord. med. tidskr. **16**:1407 (Sept. 10) 1938.

A boy aged 8 years, suffering from prolonged meningococcic septicemia with meningitis, was treated without success with sulfonamide, repeated injections of specific serum and suboccipital punctures. Continuous drainage of the cerebellomedullar cisterna by means of the puncture needle was eventually followed by recovery.

WALLGREN, Göteborg, Sweden.

ENCEPHALITIS ASSOCIATED WITH VARICELLA. ROLF BERGMAN, Nord. med. tidskr. **16**:1484 (Sept. 17) 1938.

A boy aged 7 years showed signs and symptoms of meningeal irritation on the fifth day after the eruption of varicella. He was first seen the next day. He was then somnolent. The spinal fluid contained 100 cells (64 per cent polynuclears per cubic millimeter). The temperature was subfebrile. One week later the symptoms became slighter. Recovery ensued. Brief mention is made of 8 additional cases of encephalitis associated with varicella seen at the hospital for epidemic diseases in Stockholm from 1927 to 1938. One of these cases ended fatally.

WALLGREN, Göteborg, Sweden.

Acute Infectious Diseases

A New Effective Parasiticide in Giardiasis. L. M. Morrison and W. A. Swalm, Am. J. Digest. Dis. **6**:325 (July) 1939.

This is a report of a clinical observation: Atabrine is the most effective parasiticide available in the treatment of giardial infestation. This corroborates the opinion of many Europeans, notably Galli-Valerio, of Lausanne, Switzerland.

No control studies were used by the authors, but they report 90 per cent efficacy in a small but carefully controlled group of giardia-infested patients.

The treatment is extremely simple, inexpensive and apparently nontoxic. No dosages are given in this report.

Morrison, Savannah, Ga.

Viruses and Virus Diseases. T. M. Rivers, Bull. New York Acad. Med. **14**:383 (July) 1938.

This paper is a review of the nature of viruses. It discusses the history, progress and importance of the subject. The chemical and clinical implications are submitted, and the theoretic and practical phases are evaluated. The author concludes: "Some of the viruses may be infinitely small living organisms, the midgets of the microbial world, possessed of a nature similar to that of living entities of sorts already known, ordinary bacteria and unicellular animals, differing from them only in respect to size; others may represent forms of life unfamiliar to us; while still others may be inanimate transmissible incitants of disease. One, two or all three of these possibilities may be found to hold."

Jahr, Omaha.

Treatment of Hemolytic Streptococcus Infections and the Newer Applications of Sulphanilamide. R. Ottenberg, Bull. New York Acad. Med. **14**:453 (Aug.) 1938.

This is a comprehensive review of present knowledge of the nature of the streptococci, including the classification, the physiology and the general behavior of the various groups of the streptococci, with special reference to their toxic processes.

The treatment of the numerous streptococcic infections is discussed, including the effects of antitoxins and convalescent serums, as well as the chemotherapy, particularly that relating to sulfanilamide. The latter discussion includes a clinical evaluation of the drug, the indications for it, the dosage and precautions necessary in its administration. The use of sulfanilamide in the treatment of infections caused by other micrococci is also evaluated.

Jahr, Omaha.

Rheumatic Fever. B. H. Archer, New York State J. Med. **38**:1177 (Sept. 1) 1938.

Archer reports on 163 cases of rheumatic fever observed in the medical and pediatric services of the Lincoln Hospital. The average age of patients is 18 years, the youngest being 5. Chorea occurred in 14 in this series. Carditis was found in 122. Pericarditis occurred in 10. Subcutaneous nodules were found in 6. A large percentage of the patients had had tonsillectomy prior to their initial or recurrent attacks of rheumatic fever. There were 58 tonsillectomized patients (39 per cent). It was found that a preceding infection of the throat or of the upper respiratory tract had occurred in 43 per cent of the patients. No evidence was found to justify tonsillectomy as a prophylactic or a curative measure for rheumatic fever.

Aikman, Rochester, N. Y.

Diet in Rheumatic Diseases. J. A. Nixon, Brit. J. Phys. Med. **1**:353 (Oct.) 1938.

The author does not believe that diet is of material importance in the causation and course of acute rheumatism in childhood. However, he recommends a diet rich in protein as well as in iron in the management of the disease.

Hartman, Cleveland.

THE NATURE OF GROWING PAINS AND THEIR RELATION TO RHEUMATISM IN CHILDREN AND ADOLESCENTS. J. C. HAWKSLEY, Brit. M. J. **1**:155 (Jan. 28) 1939.

Hawksley does not feel that "growing pains" and pains of rheumatism are due to the same etiologic factor. Attention is drawn to the necessity of a careful diagnosis from the history, the results of physical examination, and so on. The sites of the pains are different, the pains of rheumatism being in the joints and "growing pains" usually along the tendons and the muscles. Tenderness is rare in the course of "growing pains." In "growing pains" orthopedic posture is considered of more importance than any possibility of rheumatic infection. In the course of "growing pains" nodules do not occur. They do occur in rheumatism. "Growing pains" do not produce fever or tachycardia, but rheumatic pains of the joints produce both. In "growing pains" there is no anemia. Anemia is common in rheumatism. There is no antecedent infection of any kind demonstrable in "growing pains." In rheumatism it is usually demonstrable. Electrocardiograpic study will determine the cause of the rheumatic pains but not that of "growing pains."

ROYSTER, University, Va.

THE DENGUE EPIDEMIC OF 1937 IN CAIRO. A. W. WAKIL and F. HILMY, J. Egyptian M. A. **21**:716 (Nov.) 1938.

Wakil and Hilmy report an epidemic of dengue fever that occurred in Cairo in 1937. Dengue had been a reportable disease in Egypt since 1928, though this fact had not been generally understood. The first reports came in during October 1937. Study revealed that the epidemic had begun in September 1937. It waned by the beginning of the New Year. There were 2,594 cases reported, with 50 deaths. The authors feel that the total number of cases was actually around 400,000, as judged by the absentee records of schools and industries. The epidemic in Cairo was unique in that its origin could not be definitely fixed. There was no similar condition in the other countries with which Egypt is closely connected by land, sea or air. Nor were other provinces of Egypt affected. It is significant that sporadic cases had been recorded in Egypt and even in Cairo each year since the previous epidemic in 1927-1928. There is included a historical sketch of dengue fever in Egypt.

MULHERIN, Augusta, Ga.

COMBINED SERUM AND SULPHANILAMIDE IN THE TREATMENT OF STREPTOCOCCAL INFECTIONS IN MICE. H. LOEWENTHAL, Lancet **1**:197 (Jan. 28) 1937.

A single dose of sulfanilamide administered at the time of infection with hemolytic streptococci protected only a minority of normal mice, whereas it protected the majority of animals which received a dose of antiserum sixteen to eighteen hours before infection.

Mice infected with hemolytic streptococci can be effectively treated with a combination of sulfanilamide and antiserum even if this treatment is begun as long as eighteen hours after infection, when the animals are already severely ill. The two therapeutic agents act in a different but complementary manner.

LANGMANN, New York.

COMPLICATIONS OF ANTIRABIC VACCINATION; RARE PSYCHIC FORM OF ENCEPHALITIS AND OCULOMOTOR PARALYSIS; FAVORABLE EVOLUTION. C. SARROUY, Bull. Soc. pédiat. de Paris **36**:467 (July) 1938.

A girl 10 years old was given antirabic vaccination after a slight dog bite on the leg. She became ill on the day of the fifteenth injection, which was the last. There were psychic disturbance and transitory paralysis of the right external rectus muscle with diplopia. She recovered gradually in eight days. No sequelae occurred.

BENJAMIN, Montreal, Canada.

PRIMARY SEPTICEMIA DUE TO PFEIFFER'S BACILLUS IN AN INFANT FOUR MONTHS OLD. R. POINSO, J.-E. PAILLAS and H. MONGES, Bull. Soc. pédiat. de Paris **36**:480 (July) 1938.

A girl had infection of the upper respiratory tract and of the left elbow joint. Pfeiffer's bacillus was recovered in cultures of the blood as well as from fluid aspirated from the elbow joint. Necropsy revealed no definite pneumonia, although the lungs were congested. The liver, spleen and kidneys were also congested, and there was hemorrhage in the medullary portions of the adrenals.

BENJAMIN, Montreal, Canada.

MALARIA SIMULATING ACUTE ABDOMINAL CONDITIONS. L. D. RABINOVICH and X. S. ZISMAN, Vrach. delo **20**:746 (Oct.) 1938.

The authors present 11 cases of malaria with symptoms simulating acute abdominal disease. Three of the patients were children from 11 to 12 years of age, the rest being young and old adults. A history of previous attacks of malaria was obtained in only 2 instances. Most of the patients presented the clinical picture of acute appendicitis. Two patients, 1 of them a child aged 11 years, were subjected to appendectomy. The spleen was palpable in 1 patient only, on the first day of the disease, and in 3 patients on the second and third day. The diagnosis of malaria was confirmed by the finding of Plasmodium malariae in all 11 patients as well as by rapid disappearance of symptoms when the specific therapy was instituted.

The authors bring out the following important differential points: first, the sudden onset of the attack with marked elevation of temperature in all of these cases; second, definite periodic fluctuation in the severity of the symptoms, and third, absence of leukocytosis in most instances.

Although pathologic changes have been observed in the intestinal organs of patients with malaria, the authors believe that the clinical picture just described is best explained on the basis of general malarial intoxication, as would appear from the sudden and prompt disappearance of the aforementioned symptoms.

A true difficulty is presented by the patient with chronic malaria who may simultaneously have an acute abdominal condition. The authors point out that, although it is essential to rule out malaria in all cases of acute abdominal disease, it must not be forgotten that a patient with chronic malaria may coincidentally be suffering from an acute abdominal condition. BODER, Los Angeles.

SEPTICOPYEMIA SUCCESSFULLY TREATED BY INTRAPERITONEAL BLOOD TRANSFUSIONS. CARL FRIDERICHSEN, Nord. med. tidskr. **15**:703 (April 30) 1938.

A breast-fed infant aged 2 months had pyuria, pyoderma, otitis and anemia. Three intramuscular injections of blood were given, without success. After 3 intraperitoneal blood transfusions (50 cc.), recovery occurred. This mode of giving blood transfusions is recommended instead of the intravenous method, which often is difficult to use in the case of a small child. WALLGREN, Göteborg, Sweden.

Chronic Infectious Diseases

ACQUIRED SYPHILIS IN CHILDREN: CASE REPORTS ON FOUR SISTERS. A. G. SCHOCH and W. E. LONG, Am. J. Syph., Gonor. & Ven. Dis. **23**:186 (March) 1939.

The report is concerned with 4 Negro girls who were all infected by the same 17 year old boy. ROYSTER, University, Va.

PROTECTION OF MARRIAGE AND CHILDLIFE AGAINST SYPHILIS. W. F. SNOW, Am. J. Syph., Gonor. & Ven. Dis. **23**:277 (May) 1939.

This is a discursive article stating the arguments in favor of and against propaganda and legislation for the protection of mothers and children against syphilis. The article is provocative of thought, but to describe the measures proposed would consume too much space.

ROYSTER, University, Va.

THE IRREGULAR EXTENSIONS OF THE END OF THE SHAFT IN THE X-RAY PHOTOGRAPH IN CONGENITAL SYPHILIS, WITH PERTINENT OBSERVATIONS. EDWARDS A. PARK and DEBORAH A. JACKSON, J. Pediat. **13**:748 (Nov.) 1938.

Park and Jackson describe the pathologic process which in cases of congenital syphilis gives rise to a roentgen phenomenon that in some cases is striking. The roentgen picture is that of irregular projections of dense shadows of the end of the shaft into the cartilage. The ends of the long bones appear jagged, irregularly serrated or marked by wedge-shaped, thornlike or completely irregular projections, or the end of the bone appears irregularly scalloped. In the ribs the extensions into the cartilage are longer and sharper, and the appearance is often as if the rib were barbed or pronged. Underlying this picture is a pathologic process in which the cartilage in immediate proximity to the cartilage-nutrient canals matures much more rapidly than is normal and remains more nearly normal in appearance, whereas the cartilage at a distance from the cartilage canals does not or undergoes a degenerative process. In the cartilage around the canals, calcification occurs faster than normal, whereas between the canals it occurs much more slowly or not at all. Lattice formation (calcification of the matrix frame) occurs around the cartilage canals in advance of lattice formation between. The projections are the result of the extensions of the lattice around the canals, and they are rendered more prominent by the lagging or failure of calcification in the regions between.

RAUH, Cincinnati.

MODERN VIEWS ON THE PREVENTION OF TUBERCULOSIS. D. M. DUNLOP, Brit. M. J. **2**:1297 (Dec. 24) 1938.

Dunlop feels that one should make every effort to prevent the primary tuberculous infection in the child and likewise that massive infection in the child should be avoided if possible. Children should be segregated from close contact with persons having open tuberculosis, and a clean milk supply should be provided. There are several environmental problems which should be met and corrected. Among them are defects of housing, nutrition and habit and intercurrent infections. All of these he believes induce tuberculous infection. As may be surmised, he feels that the solution of the problem is through education.

ROYSTER, University, Va.

ERYTHEMA NODOSUM ASSOCIATED WITH ACUTE TUBERCULOUS CERVICAL LYMPHADENITIS. B. C. THOMSON, Brit. M. J. **1**:159 (Jan. 28) 1939.

Erythema nodosum associated with acute tuberculosis of cervical lymph nodes is described as observed in 6 children. In 3 the tuberculous infection is believed to have been recent and the bacilli to have gained entrance by way of the tonsil, septic follicular tonsillitis having been contributory to this invasion and possibly also to the subsequent softening and suppuration of the tuberculous lymphadenitis. In the other 3 patients tuberculosis was known to have been present for a number of years. The exacerbation in cervical lymph nodes concurrent with the onset of erythema nodosum is attributed to reactivation of tubercle bacilli latent in the lymph nodes in 2 patients and in the pulmonary parenchyma in the third, though the possibility of exogenous superinfection must be admitted.

The genesis of the cutaneous lesions is discussed, and their identity as hematogenous tuberculous foci is suggested by the concomitant phlyctenular keratoconjunctivitis in 2 patients.

The associated lesions of skin and eye underwent exacerbation and remission more or less coincidently. On the other hand, in 3 patients in whom the initial symptom was an enlargement of lymph nodes, this was observed to regress immediately following the appearance of erythema nodosum. The implications of these phenomena in relation to allergy and immunity are discussed.

ROYSTER, University, Va.

A COMPARATIVE STUDY OF THE TUBERCULIN "PATCH TEST" AND THE INTRACUTANEOUS MANTOUX TEST IN CHILDHOOD. D. COURT, Brit. M. J. **1**:824 (April 22) 1939.

The study is explained in the title, and the conclusions are as follows:

"The Vollmer patch test approaches in reliability the intracutaneous method of Mantoux.

"In a very high proportion of cases it will reveal the presence of tuberculous infection. For the remaining minority a combination of patch test and the Mantoux, using stronger concentrations of old tuberculin, or its equivalent, will prove satisfactory."

ROYSTER, University, Va.

DIAGNOSTIC VALUE OF THE INTRADERMAL TUBERCULIN TEST IN CHILDREN. D. B. BRADSHAW, Brit. M. J. **1**:825 (April 22) 1939.

Bradshaw believes that the intradermal tuberculin test is positive in almost 100 per cent of patients proved to have tuberculosis with the exception of those who are moribund. A positive reaction is proof of past or present tuberculous infection. It does not prove that active tuberculosis is present or that any given lesion is tuberculous in its origin. Its value lies largely in the exclusion of tuberculous infection. It has limited usefulness. It is determined by the percentage of positive reactions among the general population. An analysis of these tests reveals that the value of the tuberculin test is much underrated; especially is this true in regard to older children.

ROYSTER, University, Va.

ISOLATED SWELLING OF LOWER JAW CURED BY MERCURIAL TREATMENT. CHARLES RUPPE and GEORGES SÉE, Bull. Soc. pédiat. de Paris **36**:492 (July) 1938.

A girl 7 months old had a swelling of the right cheek, apparently in the lower jaw. Progressive improvement followed mercurial inunction. Despite negative serologic reactions and in the absence of any positive evidence the lesion was considered to be syphilitic on the basis of the therapeutic result.

BENJAMIN, Montreal, Canada.

EPIDEMIC OF TUBERCULOSIS IN A SCHOOL. ESCHBACH, POTHEAU and GAUCHERY, Bull. Soc. pédiat. de Paris **36**:697 (Nov.) 1938.

A girl with pulmonary tuberculosis went from one school to another. A number of classmates were found to have been infected by her. It is concluded that a thoracic roentgenogram of each pupil should be compulsory on entrance to any school.

BENJAMIN, Montreal, Canada.

TUBERCULOUS HEMORRHAGIC ENCEPHALITIS. J. BOUCOMONT and H. GUIBERT, Bull. Soc. pédiat. de Paris **36**:717 (Nov.) 1938.

A girl 13½ years old died of tuberculous meningitis. Necropsy revealed in addition a hemorrhagic infarcted area in the brain, apparently the result of thrombophlebitis of a large pial vein. Neither tubercles nor bacilli were demon-

strated in this lesion. There was evidence of diffuse subarachnoid inflammatory reaction. It is possible that there was not time enough for the usual granulomatous lesions to develop, as the terminal illness lasted only eight or ten days. A tuberculous focus was present in the lower lobe of the left lung.

BENJAMIN, Montreal, Canada.

ANTITHERMIC THERAPY IN TUBERCULOSIS. PAULO SEABRA, Imprensa méd. **13**:252 (Dec. 1) 1937.

This is an exposé of the rationale of using colloidal copper morrhuate in the treatment of tuberculosis. The theory is that the fatty acids, neutralized by the copper in order to prevent a favorable action on the growth of the tubercle bacilli, act as lyophobic colloids and adsorb the toxins from the tubercle bacilli and necrotic tissue. The preparation is given intravenously, 5 to 10 cc. three times a day. Adsorption of the toxin does much to counteract the noxious effects of tuberculous infection, and this is manifested by reduction in fever as well as by lessening of the fatigue and malaise. The author also favors treatment with the morrhuate as a preliminary to collapse therapy.

LESLIE, Evanston, Ill.

TUBERCULOSIS OF INFANTS IN LÜBECK. Časop. lék. česk. **76**:442 (April 9); 477 (April 16); 501 (April 23); 535 (April 30); 569 (May 7); 600 (May 14) 1937.

The catastrophe at Lübeck, Germany, provides a unique research opportunity, in that the exact time and circumstances of the inoculation of 251 infants with virulent tuberculosis are known. Of these, 76, or 30 per cent, died during the first year, 1 during the second year and none during the third year. This makes a death rate of 30.7 per cent for the whole series. Sixty-eight autopsies revealed that 93.5 per cent had tuberculosis, so that 28.7 per cent of the inoculated infants died of tuberculosis. Of all the infants born in Lübeck during this period, 60 per cent were immunized, and for the remaining 40 per cent there was a death rate of 9.8 per cent in the first year and 11 per cent in the second and third year; none of these died of tuberculosis. Of the 174 infants remaining alive, 6 had a permanent defect and 127 had calcified foci that were classed as clinically latent. The incubation period (to the onset of symptoms) varied from four to eight weeks. The pathologic picture, clinical symptoms, glandular and intestinal involvement, meningeal involvement, cervical adenitis, primary foci, hematogenous changes in the lungs, bacteriology, hematology and cultural characteristics are discussed. All the therapeusis attempted for the progressive condition was of no avail.

STULIK, Chicago.

GENITAL AND ABDOMINAL TUBERCULOSIS IN AN INFANT. S. GÖRANSSON, Nord. med. tidskr. **16**:1115 (July 9) 1938.

A boy aged 15 months fell ill in August 1937, with high fever. He was first seen one month later. The tuberculin reaction was positive. There was tuberculous epididymitis. A roentgenogram of the chest was normal. A fortnight later a tumor was felt at the left side of the abdomen. There was no ascites. Tubercle bacilli of the bovine type were demonstrable in the lavage water from the stomach. The boy had been fed unboiled milk from a farm during the summer.

WALLGREN, Göteborg, Sweden.

EPITUBERCULOSIS WITH DISPLACEMENT OF THE MEDIASTINUM. F. KNUTSSON, Nord. med. tidskr. **16**:1119 (July 9) 1938.

A girl aged 5 years had primary pulmonary tuberculosis on the left, with extensive parenchymatous lesions of the upper lobe. Resolution began one and one-half years later and was complete in two months. When the epituberculous

process had existed for one year an increasing displacement of the mediastinum to the left was observed, and this displacement remained after disappearance of the epituberculous lesions. The condition is considered to be due to retarded development of the left lung produced by the long-standing morbid process.

WALLGREN, Göteborg, Sweden.

VITAMIN C STANDARD FOR CHILDREN SUFFERING FROM TUBERCULOSIS OF BONES AND JOINTS. H. DAGULF, Nord. med. tidskr. **16**:1315 (Aug. 20) 1938.

By means of ascorbic acid saturation tests it is demonstrated that patients with surgical tuberculosis have a greater tendency to vitamin C deficiency than have normal persons. There is, however, no sharp limit, between physiologic and pathologic conditions, and even healthy persons may show a distinct deficiency in vitamin C. Even in healthy children the blood serum may be found free from ascorbic acid. The renal threshold value of ascorbic acid is variable in different persons and at different times in the same person, depending on the rapidity of overflowing of the blood with vitamin C. WALLGREN, Göteborg, Sweden.

MEASLES AND SURGICAL TUBERCULOSIS. GUSTAF ADOLF LANDOFF, Nord. med. tidskr. **16**:1942 (Dec. 10) 1938.

This paper is a report on the effect of measles on 18 children with tuberculosis of bones and joints and 4 children with lymphoma of the neck. In 15 cases the measles had a very light course owing to preventive convalescent serum therapy. All children were carefully observed for six months after the measles. In only 2 cases had the local tuberculosis progressed. In another case there was progression of the tuberculous lesion in the lungs, and in 3 cases there were a temporarily increased sedimentation rate of the blood, a subfebrile temperature and a decreased body weight. None of the children died.

WALLGREN, Göteborg, Sweden.

Diseases of Blood, Heart and Blood Vessels and Spleen

EXPERIMENTAL THROMBOPENIC PURPURA. L. M. TOCANTINS and H. L. STEWART, Am. J. Path. **15**:1, 1939.

The clinical and pathologic manifestations of experimental purpura as produced with antiplatelet serum in the dog undergo a uniform evolution, the stages of which may be conveniently divided into: (1) an acute stage (first to fifth days), in which occur thrombopenia, with a prolonged bleeding time, and, in the tissues, hemorrhage, edema and deposition of pigment; (2) an intermediate stage (fifth to tenth days), during which there are a rising platelet count, a short bleeding time and multiple vascular thrombi in various organs, principally in the spleen and (3) a reactive stage (after the tenth day), characterized by a high platelet count and hyperplastic changes in the bone marrow, spleen, lymph nodes, thymus and Peyer's patches of the ileum. There are indications that these evolutionary changes of the experimental disease are duplicated to a certain extent in spontaneously occurring thrombopenic purpura of man.

FROM AUTHORS' SUMMARY. [ARCH. PATH.]

EXPERIMENTAL THERAPY OF ACUTE LEUCEMIA WITH EXTRACTS OF BONE MARROW. JEAN V. COOKE, J. Pediat. **13**:651 (Nov.) 1938.

The hypothesis is suggested that acute leukemia may be related to a deficiency in physiologic factors necessary for the maturation of the granular leukocytes in the marrow. A series of experiments is reported. Children with acute leukemia were treated by injection of extracts of bone marrow in an attempt to replace

the missing factors of maturation in hemopoiesis. Of the patients treated, 4 showed more or less complete remission of the leukemic state, and in several others there was evidence of considerably increased maturation of the granular leukocytes.

RAUH, Cincinnati.

NIEMANN-PICK'S DISEASE: REPORT OF THREE CASES IN ONE FAMILY. DAVID MERKSAMER and BENJAMIN KRAMER, J. Pediat. **14**:51 (Jan.) 1939.

Three cases of Niemann-Pick's disease occurring in one family are reported. There were no normal children in the family. The parents of the children were first cousins, Jewish and born in Russia. The mother's parents were also first cousins. In 2 of the cases the cherry-red spot in the macula was present. The close resemblance of Niemann-Pick's disease to amaurotic familial idiocy is discussed.

RAUH, Cincinnati.

THE ROENTGENOLOGIC DEMONSTRATION OF ESOPHAGEAL VARICES AS A DIAGNOSTIC AID IN CHRONIC THROMBOSIS OF THE SPLENIC VEIN. HARRY M. GREENWALD and MILTON G. WASCH, J. Pediat. **14**:57 (Jan.) 1939.

The symptom complex of gastric hemorrhage, alterable splenomegaly, leukopenia and anemia has been generally accepted as the result of an obstruction in the portal or splenic veins due to thrombophlebitis of the vessels, narrowing of the splenic vein, congenital malformations of the portal or splenic veins, pressure on the veins from without or sclerosis of the vessel walls. As a result a collateral circulation is established, and esophageal and gastric varices result from overfilling of the collateral veins. Eventually the collateral circulation is taxed to such an extent that rupture of the varices occurs and the characteristic hemorrhage results. Chronic thrombosis of the splenic vein has been recognized before operation or necropsy, but only after gastric hemorrhage has occurred. It is important to recognize this disease before hemorrhage occurs because treatment (splenectomy, omentopexy and ligation of the coronary veins) early in the disease will prevent fatal hemorrhage and may prevent progress of the process with its resulting irreparable damage to the liver. Chronic thrombosis of the splenic vein can be recognized before gastric hemorrhage occurs provided the disease is kept in mind and esophageal varices are looked for in cases of unexplained splenomegaly. These esophageal varices may be demonstrated by means of roentgenograms taken after administration of a mixture of barium, powdered acacia and water. When varices are present the flow of this mixture through the esophagus is slow and the smooth normal markings are replaced by irregular defects varying in size from that of a lentil to that of a small hazelnut. "Negative" shadows are produced by the crest of the engorged veins, the barium resting in the trough of the vermicular varicose veins. Rugal markings are lost. Two case reports of the symptom complex thrombosis of the splenic vein are included in the paper. RAUH, Cincinnati.

RIGHT-SIDED AORTIC ARCH. J. P. MCGIBBON, Edinburgh M. J. **45**:620 (Sept.) 1938.

Maude Abbott found this anomaly in only 14 of 1,000 hearts with congenital disease.

McGibbon cites 3 cases. Two of the patients were adults in the fifth decade of life. One was a 15 year old girl, who was first seen at the age of 18 months. This girl had had pneumonia at the age of 3, scarlet fever at the age of 7 and diphtheria at the age of 9; at 10 years her height was 40½ inches (103 cm.) and her weight 53 pounds (24 Kg.).

The roentgen picture commonly shows a blunting of the lower part of the left border of the heart, forming a deep sharp angle with the diaphragm. The hypertrophied right ventricle causes the apex of the left ventricle to be displaced upward, while the "waist" of the heart may seem of increased depth because of the smallness of the pulmonary artery.

Right-sided arch has been reported frequently associated with Fallot's tetrad. Such was the case with this child and the two persons past middle life. The right-sided aortic arch was an isolated congenital abnormality. Roentgen pictures are reproduced.

NEFF, Kansas City, Mo.

THE USE OF PLACENTAL BLOOD FOR TRANSFUSION. A. P. M. PAGE, K. G. SEAGER and E. M. WARD, Lancet **1**:200 (Jan. 28) 1939.

Placental blood furnishes a ready and inexhaustible supply for transfusion purposes. It is preferable to ordinary adult blood because it contains no food allergens and because its clotting power is greater. No abnormal reactions are encountered during or after transfusions. Samples of blood of the same group can be mixed to provide large transfusions.

A citrate saline solution is used as anticoagulant. The umbilical cord is clamped immediately after the infant is born, without waiting for the pulsations to cease. The infant is separated from the mother. After the cord has been sterilized with alcohol a fresh cut is made, and the blood, which issues in a forcible jet, is collected in a flask. An average of 80 cc. of blood was obtained from each placenta. (The average reported by Goodall was 125 cc.) No ill effects on either mother or child were noted.

The authors state that as a rule the blood is used within two weeks, although specimens stored for over a month show a minimal degree of hemolysis.

LANGMANN, New York.

TRANSFUSION WITH PLACENTAL BLOOD. J. HALBRECHT, Lancet **1**:202 (Jan. 28) 1939.

This report is from the Beilinson Hospital in Palestine. Placental blood was used in 116 transfusions, with good results. Three and eight-tenths per cent sodium citrate solution was used as the anticoagulant. The blood was preserved in a refrigerator at 4 to 5 C. for as long as two weeks. The average yield from each placenta was 50 to 60 cc.

LANGMANN, New York.

ACUTE LEUKEMIA OF UNDIFFERENTIATED CELLULAR TYPE: ONSET WITH PAIN. G. A. PATEY and RONSIN, Bull. Soc. pédiat. de Paris **36**:638 (Nov.) 1938.

A girl 11 years old died of acute lymphatic leukemia. She had had pain in the extremities three months previously. This occurred again at the onset of the acute terminal phase of the disease, which was characterized by fever, enlargement of the lymph nodes, progressive pallor and hemorrhage. The blood contained as many as 256,000 white blood cells per cubic millimeter, 95 per cent of which were of embryonic, undifferentiated type. Necropsy was not performed.

BENJAMIN, Montreal, Canada.

PERNICIOUS ANEMIA WITH GRANULOCYTOPENIA IN A YOUNG CHILD SUFFERING FROM MEGACOLON. PIERRE BARBÉ, Bull. Soc. pédiat. de Paris **37**:47 (Jan.) 1939.

A boy 32 months old had a large abdomen and marked anemia. Fever, vomiting, abdominal pain and alternating loose stools and constipation were noted. A month later laparotomy revealed that the cecum and the colon as well as the mesenteric nodes were enlarged. The child left the hospital aften ten days. The blood picture resembled that associated with pernicious anemia. Liver and stomach extracts were administered, but the anemia became progressively worse, and the boy died a few weeks later.

BENJAMIN, Montreal, Canada.

TREATMENT OF DILATATION OF THE HEART PRODUCED BY OVERWORK IN AN ADOLESCENT ATHLETE. E. J. KLAUS, Ztschr. f. Kreislaufforsch. **31**:7 (Jan. 1) 1939.

Detailed clinical and roentgen investigation of a case of dilatation of the heart in a 16 year old boy, produced by overwork, is described. The dilatation was a longitudinal one, occurring to a higher degree in the right than in the left side of the heart. The systolic blood pressure was elevated, and the pulse pressure was increased. Normal size of the heart and normal function were observed within six weeks after training and physical exercise were discontinued.

ARON, Chicago.

OBJECTIVE AURAL BRUITS OR MURMURS. FRANK TETERA, Časop. lék. česk. **76**:527 (April 30) 1937.

Objective aural bruits are rarer than subjective ones and only about 100 cases are found in the literature. A boy aged 18 years had an aneurysm of the superficial temporal artery with a bruit which was both objective and subjective. During the past year the rumble became so disconcerting that ligation above and below the aneurysm was performed. The auditory murmur entirely disappeared. The Wassermann reaction was negative, and there was no history of previous trauma.

STULIK, Chicago.

NORMAL BLOOD OF SCHOOL CHILDREN. POUL FAERGEMAN, Nord. med. tidskr. **16**:1738 (Nov. 5) 1938.

Three hundred children 8 to 14 years of age were examined. The normal values for hemoglobin, erythrocytes and cell volume are the same as for adult healthy women. There is no difference between the two sexes, and the values are unchanged throughout the age groups examined.

WALLGREN, Göteborg, Sweden.

THROMBOPENIC PURPURA WITH LIFE-MENACING BLEEDING AT THE MENARCHE. ODD SANDAKER, Nord. med. tidskr. **16**:1740 (Nov. 5) 1938.

A 15 year old girl had numerous purpuric spots on her legs. Examination displayed thrombopenia (17,000 platelets). Thirteen days later she had her first menses, and the bleeding was so profuse that her life was in danger. Two blood transfusions did not decrease the bleeding, and splenectomy had to be performed. After the operation the bleeding stopped and the platelets increased to supernormal values, and during the two following menstrual periods the bleeding was within normal limits.

WALLGREN, Göteborg, Sweden.

Diseases of Nose, Throat and Ear

ACUTE LARYNGOTRACHEOBRONCHITIS IN CHILDREN. CHEVALIER L. JACKSON, M. Clin. North America **22**:1518 (Nov.) 1938.

Although symptomatically it closely resembles laryngotracheobronchial diphtheria, this disease is not diphtheria. Of Jackson's cases, the condition in 85 per cent was unquestionably due to streptococci. Other organisms (staphylococci and influenza bacilli) have been reported as predominant in some cases. The clinical picture is that of a more or less toxic child with a moderate or high temperature and rapidly progressive obstructive dyspnea. Absence of membrane in the oropharynx does not absolutely preclude the presence of diphtheria, and when visualization of the lower air passages is not possible it is advisable to give an injection

of serum. Serious complications, such as infection of the blood stream (especially with streptococcic conditions), subglottic edema and bronchopneumonia may occur. Obstructive atelectasis is frequently mistaken for pneumonic consolidation. Atelectatic areas quickly disappear, however, when bronchial obstruction is removed.

Until recently the mortality of the fulminating types was 50 to 70 per cent; with the employment of all modern methods of treatment, the death rate is seldom less than 25 per cent.

The two essentials of treatment are water and a free airway. Fluids must be supplied in adequate amounts by whatever means available. The child should be kept in an environment of warm, moist air and given every possible chance to rest. However, sedatives, especially opiates, should be avoided. The restless child will become quiet if his dyspnea is relieved. For the relief of obstruction, tracheotomy should be done as promptly as indicated, and the passages should be kept clear by means of suction through the tube. This will produce relief in about 50 per cent of cases. Later it may be necessary to remove hard masses, plugging the bronchi, through the bronchoscope. This may have to be done repeatedly in some cases as a life-saving measure.

EUGENE H. SMITH, Ogden, Utah.

ASSOCIATION OF STAMMERING AND THE ALLERGIC DIATHESIS. A. M. KENNEDY and D. A. WILLIAMS, Brit. M. J. **2**:1306 (Dec. 24) 1938.

Kennedy feels that there is a close association between stammering and the allergic diathesis. This diathesis may be in the child or in the family. Other associated conditions are emotional imbalance, migraine, anxiety complexes, etc. The author studied a consecutive series of 100 children who suffered from stammering. All of them except 1 had a personal or family history of symptoms indicating allergy; 52 had a personal history of allergy, and 48 of these also had a positive history of allergy. Forty-eight gave no personal history of allergy but all except 1 had a positive family history.

The various allergic manifestations in the patients and their families have been tabulated and the closeness of the allergic inheritance noted.

A family history of stammering was obtained for 65 of the 100 children, and the closeness of the stammering inheritance has been noted.

ROYSTER, University, Va.

CONGENITAL OCCLUSION OF THE POSTERIOR NASAL CHOANAE. D. B. KELLY, Brit. M. J. **1**:157 (Jan. 28) 1939.

Although rare, congenital occlusion of the posterior nasal choanae deserves consideration. In the newly born infant there is considerable difficulty of breathing, resulting in dyspnea and even cyanosis, and this is relieved only when the baby's mouth is opened as when crying. It is cyclic in its occurrence. Both sucking and nutrition are interfered with. Unilateral occurrence is rarely recognized in early life. Only when the patient is older does it come to the attention of the physician. Kelly thinks that the obstruction is caused by absorption of the bucconasal membrane. It may be either unilateral or bilateral. Its cause is considered a defect in embryonal development. A case is reported. The operative technic is outlined, and attention is drawn to the difficulty of keeping the artificial ostium made in the occluding bony plate open.

ROYSTER, University, Va.

PULMONARY COMPLICATIONS FOLLOWING TONSILLECTOMY. Z. SZOLNOKY, Monatschr. f. Ohrenh. **73**:48 (Jan.) 1939.

The author has observed the following pulmonary complications after tonsillectomy: 1. Bronchitis. Among 100 patients, only 4 had normal temperature after tonsillectomy; the remainder had a fever for six to eight days, the temperature rising to 100.4 F. This rise of temperature is explained by the author as postoperative bronchitis. Unfortunately he does not describe his technic of tonsil-

lectomy. It would be of interest to know something about that, since his finding that patients have fever for six to eight days after the operation is not in agreement with the usual experience. 2. Pneumonia. Among 3,000 operations, the author observed bronchopneumonia after 12. 3. Abscess and gangrene of the lung. This complication took place in 2 cases only. Both patients were operated on under local anesthesia and were adults.

In order to study the pathogenesis of the pulmonary abscess, the author performed the following experiments: After the surgical removal of the tonsil, he dropped 3 cc. of iodized poppyseed oil into the fossa. After two minutes, he observed the radiopaque area within the bronchi by means of a fluoroscope. He draws the conclusion from these experiments that the pulmonary abscess develops by aspiration of infectious material from the mouth into the lungs and is not produced by emboli within the blood vessels of the lungs.

LEDERER, Chicago. [ARCH. OTOLARYNG.]

THE TREATMENT OF PAINS FOLLOWING TONSILLECTOMY WITH VITAMINS B_1 AND C. M. BAER, Monatschr. f. Ohrenh. **73**:58 (Jan.) 1939.

The pains following tonsillectomy are due to the wound within the mouth. Therefore, morphine, particularly as a suppository, should be administered. The pains, which sometimes are late complaints after the operation, are combined with some disturbances in the vitamin balance. In such cases the administration of vitamins B_1 and C seems to be the suitable treatment.

LEDERER, Chicago. [ARCH. OTOLARYNG.]

SEVERE INJURY TO THE REGION OF THE MASTOID. F. X. KOCH, Monatschr. f. Ohrenh. **73**:66 (Jan.) 1939.

A girl 8 years old received a severe fracture in the region of the left mastoid process. A radical operation on the middle ear was performed, with wide exposure of the dura. An uneventful recovery followed.

LEDERER, Chicago. [ARCH. OTOLARYNG.]

CLINICAL CONSIDERATION OF CHOLESTEATOMA OF THE MIDDLE EAR AND ITS COMPLICATIONS. HELMUTH RICHTER, Ztschr. f. Hals-, Nasen- u. Ohrenh. **44**:340, 1938.

The author reports a series of 136 cases of cholesteatoma of the middle ear in patients varying in age from 1 year to 68, three quarters of them belonging in the first three decades.

In 13 cases the cholesteatoma was bilateral. The author performed 143 operations in all, 87 on the right ear and 56 on the left, but he did not attach any particular significance to the incidence on either side. Eighty-one patients were studied roentgenologically; of these, 80 showed marked limitation of pneumatization. He had 123 recoveries and 14 deaths (10 per cent).

He had an impressive series of complications (110 cases): subperiosteal abscess in 9 cases, extradural abscess in 11, perisinal abscess in 25, labyrinthitis in 27, thrombosis of the lateral sinus in 13, cerebral abscess in 4, abscess of the temporal lobe in 4 and suppurative meningitis in 17. Those in 65 were dangerous. Analysis of 62 of these 65 cases showed 48 recoveries (77 per cent) and 14 deaths (23 per cent). The organism most frequently found was Bacillus proteus (37 cases); next in frequency were the hemolytic streptococcus, Staphylococcus aureus and Staphylococcus albus; the other usual organisms were less frequent. The spinal fluid, studied in 13 cases of meningitis, was sterile in 4.

In summarizing, the author discusses the question of 14 deaths and stresses both the importance and the danger of cholesteatoma as indicated by this long list of complications. He finally urges that an early operation be undertaken whenever cholesteatoma is suspected.

PERSKY, Philadelphia. [ARCH. OTOLARYNG.]

POLYARTHRITIS, TONSILLECTOMY AND AUTOGENOUS VACCINES. LAVAL, Ztschr. f. Hals-, Nasen- u. Ohrenh. **44**:381, 1938.

The author reports the results of his treatment of a series of 20 patients suffering from polyarthritis in both the acute and the chronic form. He recommends tonsillectomy and the use of an autogenous vaccine made from the tonsils. In this small series he obtained cure in 11 cases and arrest in 2.

He believes that this form of therapy is valuable for both the acute and the early chronic form, but when permanent contractures have occurred supplemental physical therapy must be employed, and he stresses the necessity for the internist, in his treatment of rheumatic arthritis, to have the cooperation of the rhinologist.

PERSKY, Philadelphia. [ARCH. OTOLARYNG.]

THREE CASES OF CEREBELLAR ABSCESS ASSOCIATED WITH ACUTE PURULENT OTITIS MEDIA. JOHN HYBASEK, Časop. lék. česk. **76**:549 (May 7) 1937.

Cerebellar and cerebral abscesses are murch rarer with acute than with chronic otitis, as is shown by the statistics gathered by Kolmijcenko, in which 85 per cent followed chronic otitis. The cases cited are those of a man aged 42, a girl aged 7 years and a boy aged 16 years. In these the cerebellar abscess was diagnosed five weeks, three months and nine days, respectively, after onset of otitis. The extension in the first and third cases was through formation of a perisinal abscess, periphlebitis and pachymeningitis. In the second case the extension traveled through the internal auditory canal. The patients in the first and third cases made apparently complete recoveries in seven weeks; the patient in the second case died of diffuse purulent meningitis.

STULIK, Chicago.

RESULTS OF EMERGENCY TRACHEOTOMY FOR FOREIGN BODY OF THE AIR PASSAGES IN CHILDREN: TWO CLINICAL CASES. A. LAMBESCU, Med. inf., Rumania **1**:166 (March-April) 1939.

Lambescu, after classifying the solid foreign bodies that may fall into the larynx and tracheal tube, explains the symptomatic picture and the elements of diagnosis. The discussion of the treatment occupies the greatest place and is directed first toward the extremely dramatic situation in which one is obliged without hesitation to practice tracheotomy as an emergency measure and second to the situation less pressing in which it is convenient to resort to a tracheobronchoscopic procedure. In order to avoid complications, one should not neglect any details of technic.

By means of tracheotomy, the author has saved 2 children with obstruction of their respiratory paths. If the foreign body is not embedded, one can replace the bronchoscopic approach with tracheotomy when one does not have access to a bronchoscope or to a specialist in this form of practice. It is the method to be preferred when asphyxia is acute. At other times tracheotomy should be the preliminary procedure. For children the operation of choice should be high tracheotomy under local anesthesia.

FROM THE AUTHOR'S SUMMARY.

FATAL FIBRINOUS LARYNGITIS AND TRACHEITIS. FRITIOF LEEGAARD, Nord. med. tidskr. **16**:1566 (Oct. 1) 1938.

An 8 year old boy fell ill after a slight common cold with signs of laryngeal stenosis, which in the beginning was diagnosed as pseudocroup. He had fever (temperature 40.2 C.). There was no cyanosis and no pharyngitis. The mucous membrane of the subglottic trachea was swollen. During the night there were suddenly increased symptoms of stenosis followed by loss of consciousness. Tracheotomy was performed, without success. At postmortem examination membranous laryngotracheitis was demonstrated. Hemolytic staphylococci were demonstrated. There was no diphtheria. Death was considered due to cardiac paralysis caused by the septic condition.

WALLGREN, Göteborg, Sweden.

Diseases of Lungs, Pleura and Mediastinum

BRONCHOPLEURAL-CUTANEOUS FISTULA (REPORT OF TWO CASES TREATED WITH A PEDICLE FLAP FROM LATISSIMUS DORSI MUSCLE). I. E. SIRIS, New York State J. Med. **38**:1213 (Sept. 15) 1938.

One of the patients was a boy of 15 years who had pneumonia and empyema ten months before, followed by a bronchopleural-cutaneous fistula. The fistula was successfully closed when a large pedicle of latissimus dorsi muscle with an adequate base was mobilized and placed in the exposed cavity.

AIKMAN, Rochester, N. Y.

TYPE I PNEUMOCOCCUS PNEUMONIA (OBSERVATIONS FROM STUDY OF TWO THOUSAND CASES TREATED WITH SPECIFIC SERUM). E. S. ROGERS and M. E. GOOCH, New York State J. Med. **38**:1369 (Nov. 1) 1938.

Among 158 children under 9 years of age who were treated with serum, 2 died. Of 46 children who received no serum, none died. However, Rogers feels that children tolerate serum well and reports that they have responded with surprising rapidity to small doses, with little difficulty in administration.

AIKMAN, Rochester, N. Y.

VARIATIONS IN PULMONARY VITAL CAPACITY IN HEALTH: DAILY, SEASONAL, AND AT MODERATE ALTITUDES. F. L. APPERLY, Proc. Soc. Exper. Biol. & Med. **40**:294 (Feb.) 1939.

True vital capacity diminishes at moderate altitudes, even that of 3,000 feet. This diminished vital capacity at higher altitudes is believed to be due to dilatation of the capillaries of the lungs following partial loss of external (atmospheric) support, with consequent diminution of air space. Such an increase of blood in the lungs may be a factor in the favorable effect of moderate altitudes on certain forms of pulmonary tuberculosis.

HANSEN, Minneapolis.

SINGLE LARGE CYST OF THE LUNG SIMULATING A HIGH-PRESSURE PNEUMOTHORAX. E. H. HUDSON, Brit. M. J. **1**:503 (March 11) 1939.

Hudson reports a case of cyst of the lung and emphasizes certain dangers: first, faulty diagnosis and, second, infection of the cyst.

ROYSTER, University, Va.

PULMONARY ABSCESS CURED BY INTRAVENOUS INJECTIONS OF SODIUM BENZOATE. MARIE and MICHEL CAMNER, Bull. Soc. de pédiat. de Iasi **9**:39, 1938.

An 8 year old boy seriously ill with a pulmonary abscess for thirty days was given daily injections of a 10 per cent solution of sodium benzoate. Two grams of the solution was given the first day, 3 Gm. the four succeeding days and 4 Gm. daily afterward until twenty-one doses had been given. Complete recovery occurred.

LESLIE, Evanston, Ill.

CHYLOUS PLEURAL EFFUSION IN A CHILD 2 YEARS OLD. PAUL GIRAUD, POINSO, SALMON and MOCKERS, Bull. Soc. pédiat. de Paris **36**:488 (July) 1938.

A girl 2 years old who had a positive tuberculin reaction and whose thoracic roentgenogram showed enlargement of the right paratracheal nodes and thickening of the right interlobar fissure had an effusion in the left hemithorax. Aspiration on three occasions yielded chylous fluid, in which no micro-organisms were demonstrable by smear or culture. It is thought that there was a tuberculous inflammatory element to account for the effusion and that pressure on the thoracic duct by enlarged lymph nodes could account for its rupture and entrance of its contents into the pleural cavity.

BENJAMIN, Montreal, Canada.

TREATMENT OF DILATATION OF THE BRONCHI IN CHILDREN. J. BOISSERIE-LACROIX, Paris méd. **2**:429 (Dec. 3) 1938.

A long, detailed article discusses the various methods of treating bronchiectasis. The discussion is divided into (1) medical methods, which may be applied by the general practitioner; (2) endoscopic methods, reserved for the otolaryngologist, and (3) surgical methods, which divide themselves into two classes, those aiming to obtain immobilization of the lung and those in which removal of the infected portion of the lung becomes necessary. LESLIE, Evanston, Ill.

PNEUMONIA IN GUINEA PIGS AND COMPARATIVE INVESTIGATIONS REGARDING GRIPPAL PNEUMONIA IN MAN. W. GRIESHAMMER, Arch. f. Hyg. **121**:102 (Nov.) 1938.

This is a description of an epidemic disease in guinea pigs which pathologically and anatomically showed close resemblance to human epidemic influenza, and by its bacterial causation permitted the cautious conclusion that the course was influenced by factors similar to those active in human influenza.

FALKENHEIM, Rochester, N. Y.

CONGENITAL BRONCHOGENIC CYSTS OF THE LUNG. P. COKKALIS, Deutsche Ztschr. f. Chir. **251**:400 (Dec.) 1938.

The author presents a general discussion of the symptoms and pathologic picture of pulmonary cysts, with a report of 3 cases. Extirpation of a portion of the cyst wall and drainage, rather than pneumonectomy, is advised.

HARRIS, Durham, N. C.

BRONCHIAL ASTHMA WITH RESOLVING PULMONARY CONDENSATIONS. BERTIL SÖDERLING, Nord. med. tidskr. **16**:1161 (July 16) 1938.

A girl aged 12 years had typical asthmatic attacks. The tuberculin test (1 mg.) elicited a negative reaction. No eosinophilia was observed in the blood. Eosinophils were present in the sputum. At roentgen examination a rather marked pathologic shadow was observed at the hilus of the left lung. A few days later this shadow had disappeared, but a new one was noted, involving the middle lobe of the right lung. Two days later even this shadow had disappeared. The shadows were considered to be due to atelectasis. WALLGREN, Göteborg, Sweden.

ACUTE NONTUBERCULOUS ABSCESSES OF THE LUNGS IN CHILDREN. BERTIL HAMNE, Nord. med. tidskr. **16**:1727 (Nov. 5) 1938.

The author reports 4 cases of solitary pneumonic abscess of the lungs with spontaneous recovery and 2 cases of multiple abscesses with fatal outcome. In the latter 2 cases the abscesses were associated with general sepsis, in 1 of them originating from tonsillitis. In addition, a case of interlobar empyema with rupture into a bronchus is mentioned. Clinically the condition resembled a pulmonary abscess. Recovery occurred. Emphysema blebs are discussed from the point of view of differential diagnosis. Clinically the conditions may be similar to metapneumonic abscesses of the lungs. WALLGREN, Göteborg, Sweden.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

INSPISSATION OF SECRETION, DILATATION OF THE DUCTS AND ACINI, ATROPHY AND FIBROSIS OF THE PANCREAS IN INFANTS: A CLINICAL NOTE. KENNETH D. BLACKFAN and CHARLES D. MAY, J. Pediat. **13**:627 (Nov.) 1938.

Blackfan and May describe the clinical manifestations in the cases of 35 infants in whom an advanced pathologic lesion of the pancreas was observed at necropsy. The lesion is characterized by inspissation of secretion, dilatation of the ducts

and acini, atrophy and fibrosis. In addition, chronic pneumonia of the interstitial type was observed. The clinical manifestations began early in life. Five infants died within the first few days of life. In the others the signs of a disorder of nutrition developed early in life, the average onset of symptoms occurring at about 2 months. The symptoms were usually referable to the gastrointestinal or the respiratory tract. In 7 cases the clinical picture was similar to that of celiac disease, with emaciation, distention of the abdomen and large, pale putrefactive "fatty" stools. The average duration of illness in those living beyond the neonatal period was six months, and the average age at death was 8 months.

RAUH, Cincinnati.

OBSERVATIONS ON CONGENITAL MEGACOLON. GÉZA DE TAKÁTS and ALFRED D. BIGGS, J. Pediat. **13**:819 (Dec.) 1938.

Takáts and Biggs present a discussion on the pathogenesis, diagnosis and medical and surgical management of congenital megacolon. Nine case histories are summarized. Medical treatment is recommended for children under 4 years of age, for children with mild involvement and prior to operation (sympathectomy). This treatment consists of daily irrigations, rectal dilatations and drugs which act on the parasympathetic nerves.

RAUH, Cincinnati.

ACUTE APPENDICITIS WITH JEJUNAL INTUSSUSCEPTION AND ABDOMINAL LYMPHADENITIS (OCCURRING IN A CHILD IMMOBILIZED IN A SPICA PLASTER CAST: REPORT OF CASE). ALBERT LESSER and LOUIS R. KAUFMAN, New York State J. Med. **38**:1285 (Oct. 1) 1938.

A 6 year old white boy had been in a full spica plaster cast for a fracture of the left femur and right tibia for one month when abdominal pain, constipation and vomiting occurred. During this time he was transferred to another hospital. Rectal examination revealed a large amount of impacted feces, but the abdominal pain and vomiting persisted after an evacuation by enema. No blood was found in the stool. A portion of the cast was removed, and the entire right side of the abdomen was found to be rigid and tender. The upper part of the abdomen was distended. A laparotomy revealed a gangrenous appendix and an intussusception involving about 5 inches (12.5 cm.) of the jejunum. The patient made an uneventful recovery.

AIKMAN, Rochester, N. Y.

RETROGRADE INTUSSUSCEPTION OF CECUM INTO ILEUM. E. S. GOODYEAR, New York State J. Med. **38**:1397 (Nov. 1) 1938.

A breast-fed baby was found to have retrograde intussusception of the cecum, appendix and distal portion of the terminal ileum into the more proximal portion of the terminal ileum. The intussusception was successfully reduced, but the child died four days later. This type of intussusception is seen frequently post mortem but is rarely found during life.

AIKMAN, Rochester, N. Y.

"MEDICAL APPENDIX" IN CHILDREN AND ADULTS. R. MILLER, Brit. M. J. **1**:56 (Jan. 14) 1939.

This is an abstract of a lecture given before the Bath, Bristol and Somerset Branch of the British Medical Association at Atunton on Nov. 2, 1938.

The term "medical appendix" is used by Miller to describe various signs and symptoms originating in the appendix that may not necessarily mean a surgical emergency. Abdominal symptoms arising from an appendix are due to obstruction or inflammation of the appendix. Each condition predisposes to the other. Pain is the common symptom. Localized pain occurs only when the inflammatory process has reached a certain degree. Up to this time the pain or discomfort is usually in the region of the umbilicus, but when the acute inflammation begins

the pain shifts to the right side and is accompanied by spasm of the muscles and tenderness. In children "medical appendix" manifests itself in two types, the dyspeptic type and the acidotic type. The dyspeptic type has pain referred to the umbilicus, of a colicky nature. It comes on at any time but more commonly at mealtime. The child may double up. In the acidotic type the symptoms are severe and illness more definite. It is usually sooner or later followed by vomiting. The attack may last some hours but is usually better after twelve hours' rest or sleep. This is often diagnosed as acidosis. A careful history is necessary, and not infrequently it is wise to have a roentgenogram of the gastrointestinal tract. The author also considers this condition in the adult, but that part of this article is not pertinent to this abstract.

ROYSTER, University, Va.

TOXIC STATES IN DIGESTIVE DISTURBANCES OF EARLY INFANCY. M. CAMNER, Bull. Soc. de pédiat. de Iasi **9**:28, 1938.

In a study of 41 cases, the author found that the polypeptids in the blood increased with increasing toxicity. Death occurred in 29 cases, in almost all of which the polypeptids were very high.

LESLIE, Evanston, Ill.

ENCEPHALITIC MANIFESTATIONS IN DIGESTIVE DISTURBANCES OF INFANCY. M. CAMNER, Bull. Soc. de pédiat. de Iasi **9**:34, 1938.

Two cases of severe diarrhea and one of Shiga dysentery in which neurologic disturbances were prominent are reported. Disorientation, convulsive movements, somnolence and strabismus were prominent features. The cerebrospinal fluid was essentially normal. The blood polypeptids were increased.

LESLIE, Evanston, Ill.

CONGENITAL ICTERUS DUE TO MALFORMATION OF THE BILIARY PASSAGES. R. A. MARQUÉZY, P. RAMBERT and P. GAUTHIER-VILLARS, Bull. Soc. pédiat. de Paris **36**:485 (July) 1938.

A boy 5 months old had suffered from jaundice since birth. His general condition was good. The stools were whitish, and the urine was bile stained. The blood contained excessive bile pigment but not bile salts. The liver was enlarged. At necropsy a small, contracted gallbladder was observed. It contained a small amount of clear, viscid fluid. Two hepatic ducts joined, forming a small cyst on the under surface of the liver, and this contained a small amount of fluid. There was no main hepatic duct and net even a fibrous cord running to the ampulla of Vater. The cystic duct ran directly to the ampulla. Histologically the liver showed biliary cirrhosis with considerable increase of the bile canaliculi, which were all of small caliber and many of which were obliterated by the bile pigment in them. All the organs were bile stained. The lungs showed no areas of bronchopneumonia but were congested and edematous in spots.

BENJAMIN, Montreal, Canada.

DOLICHOCOLON; ARREST OF DEVELOPMENT. P. MAYNADIER, Bull. Soc. pédiat. de Paris **36**:709 (Nov.) 1938.

A boy 3½ years old had had periods of diarrhea for some time. Roentgen examination showed a redundant sigmoid. The child was only 71 cm. tall. He weighed 8,530 Gm.

BENJAMIN, Montreal, Canada.

LIMITS OF PYLORIC DISEASE. J. BOUCOMONT and H. GUIBERT, Bull. Soc. pédiat. de Paris **36**:722 (Nov.) 1938.

A girl vomited some of her feedings in the very early days of life. Gastric peristaltic waves were observed on one occasion. Several times a tube passed into the stomach before feeding showed no retention. Tincture of belladonna was

administered before feedings for a period. The infant gained weight consistently. At 6 months of age she was operated on because of the presence of an abdominal mass. This was found to be due to an ovarian cyst which was twisted on its pedicle. The infant had a severe cutaneous infection and died after a few days. An interesting observation at necropsy was a large pylorus which on section showed marked hypertrophy of muscle and mucosa.

BENJAMIN, Montreal, Canada.

INTRAPERITONEAL INJECTIONS IN PRACTICAL PEDIATRICS. M. ABBATE, Lattante **9**:548 (Dec.) 1938.

In the Orphanage of the Annunciation in Naples, Italy, over 200 intraperitoneal injections have been given. Physiologic solution of sodium chloride and isotonic and hypertonic solutions of dextrose have been used. Abbate concludes that the method is absolutely without danger and technically easy and that it deserves more widespread use in hospital pediatrics.

HIGGINS, Boston.

HYPERTROPHIC PYLORIC STENOSIS. M. O. COSTA, Pediatria prat. **9**:295 (July-Aug.) 1938.

An orthodox review of the pathogenesis, symptoms, pathologic picture and treatment of pyloric stenosis introduces the presentation of a case. It is of interest that in the discussion of medical treatment the author mentions the use of 0.001 to 0.002 mg. doses of procaine hydrochloride "to anesthetize the stomach mucosa." The relative frequency of pyloric stenosis in first-born children (50 per cent of all cases) is stressed. The author's patient was a first-born English child who made an uneventful recovery after operation. The great rarity of pyloric stenosis in Brazil is vouched for by this report of a single case.

DIETRICH, Beverly Hills, Calif.

CONGENITAL DIAPHRAGMATIC HERNIA. M. GEORGESCU, T. NICULESCU and D. GAVRILIU, Med. inf., Roumania **1**:184 (March-April) 1939.

With respect to a congenital diaphragmatic hernia appearing in an infant of 20 months and diagnosed when first seen, the authors discuss the question of the formation of such a hernia and the difficulties of diagnosis. Two factors enter into the production of this condition, the formation of the diaphragm in two layers and its evolution in the embryonic and fetal period. The most complete classification, based on anatomic and clinical impressions, is that of Marks, included in which one finds congenital hernias. In a case observed by the authors a congenital diaphragmatic hernia had occurred in a manner most frequent—through the aqueduct of Bochdalek. They give the clinical facts and describe in detail the roentgen examination. In discussing the difficulty of diagnosis, they call attention to the different abdominal and thoracic abnormalities with which one might confuse diaphragmatic hernia. In the present case the diagnosis was made at the time of the consultation. The child was operated on but died seven hours afterwards. To conclude, the authors bring out the importance of strict collaboration between the clinician and the roentgenologist in order to make an early precise diagnosis. As to the roentgenologic examination, they affirm, in agreement with Marks, that it should be carried out in three positions: vertical, horizontal and Trendelenburg.

AUTHORS' SUMMARY.

SUCCESSFULLY REDUCED HIATUS HERNIA. ERNST BERGENFELDT, Nord. med. tidskr. **16**:1170 (July 23) 1939.

A boy aged 1½ years, who had suffered from intermittent anorexia and abdominal pains with ileus-like attacks since the age of 3 months, fell ill with hematemesis. Roentgen examination revealed a hiatus hernia. The boy was operated on and was still free from symptoms fourteen months later.

WALLGREN, Göteborg, Sweden.

TRAUMATIC RUPTURE OF THE PANCREAS IN CHILDREN. EINAR PERMAN, Nord. med. tidskr. **16**:1473 (Sept. 17) 1938.

Perman has observed 1 case of traumatic rupture of the pancreas and has collected 7 previously reported cases. In 7 cases the rupture was caused by lesions produced in accidents while riding on bicycles. In the eighth case the child had been trodden on in the epigastric region by a cow. In typical cases there is a free interval between the trauma and the signs and symptoms, depending on the fact that the latter are caused by irritation by the pancreatic juice. The result is a picture of acute pertonitis. The treatment consists in laparotomy with drainage of the omental bursa. In the 8 cases reported recovery occurred. The author's own patient, a boy aged 8 years, was operated on on the twelfth day and was discharged healthy six months later.

WALLGREN, Göteborg, Sweden.

Nervous Diseases

COMPLETE AGENESIS OF THE CORPUS CALLOSUM. DAVID L. REEVES and CYRIL B. COURVILLE, Bull. Los Angeles Neurol. Soc. **3**:169 (Dec.) 1938.

Reeves and Courville report 4 cases of complete agenesis of the corpus callosum, in all of which the diagnosis was made at autopsy. The 4 patients were aged 19 years, 3 months, 4 months and 69 years, respectively. The first patient died of subdural hemorrhage two months after a fall on the occiput, the second of unstated causes, the third of hydrocephalus and the fourth of cerebral thrombosis and hemorrhage from a duodenal ulcer. No definite mental or neurologic abnormalities had been recorded which could be attributed to the developmental defect. Other associated anomalies were discovered, including primitive radial arrangement of the sulci of the medial surface of the cerebral hemispheres, nonunion of the calcarine and parieto-occipital sulci, excessive development of the anterior commissure (although this structure was almost totally absent in case 2) and abnormally separated and dorsally blunted anterior horns and dilated posterior horns of the lateral ventricles. In the first case an extensive arachnoid cyst was observed between the hemispheres, occupying the normal location of the corpus callosum, and in the second a similar small cyst was seen above the posterior portion of the third ventricle. In the third case advanced internal hydrocephalus was present. Reeves and Courville point out that the corpus callosum develops during the third and fourth months of fetal life, and that factors leading to its agencies must operate at or before that period. Actual etiologic agents are unknown. Clinical and experimental destruction of the corpus callosum in man and animals has served to minimize the functional importance of the corpus callosum, as has the absence of any characteristic symptoms in cases of agenesis.

MACKAY, Chicago. [ARCH. NEUROL. & PSYCHIAT.]

THE HISTOPATHOLOGY OF CONVULSIVE DISORDERS IN CHILDREN. H. M. ZIMMERMAN, J. Pediat. **13**:859 (Dec.) 1938.

Extensive necrobiotic changes of the ganglion cells were found in the cerebral cortex, especially the cornu ammonis formations of the temporal lobes, the basal ganglions and the cerebellar cortex of a group of 16 children ranging in age from early infancy to 6½ years. Severe convulsions and prolonged periods of respiratory difficulty or asphyxia dominated the clinical picture in these cases. Although 7 of the children had an underlying infectious illness which suggested the possibility of encephalitis as the cause of the symptoms, the other 9 were free from infection. None of the children had inflammatory cerebral lesions which could have accounted for the symptoms. Zimmerman concludes that cerebral anoxemia resulting from the convulsions, the respiratory difficulty or the asphyxia was responsible for the lesions in the nervous system.

RAUH, Cincinnati.

ELECTRO-ENCEPHALOGRAPHIC LOCALIZATION OF ATROPHY IN THE CEREBRAL CORTEX OF MAN. M. A. RUBIN, Proc. Soc. Exper. Biol. & Med. **40**:153 (Feb.) 1939.

Electroencephalograms were taken from two to four times for 14 patients with psychotic symptoms. The relationships between the major architectonic regions of the cerebral cortex in "normal" man have been described in terms of their alpha wave (10 per second) activities (*J. Neurophysiol.* **1**:313, 1938). The method consists in determining the amount of alpha wave activity (per cent time alpha) in both hemispheres simultaneously from electrodes placed in seven standard positions along the head about 3 cm. to either side of the midline. Records from 6 patients showed one or more cortical regions in which the per cent time alpha increased in one hemisphere and decreased in the other, although the electrical activity of both hemispheres ran parallel in the adjacent regions. This was taken as a sign of atrophy. The findings were confirmed by pneumoencephalograms in 8 of 9 cases.

HANSEN, Minneapolis.

AKINESIA AFTER VENTRICULOGRAPHY. M. GROTJAHN and T. M. FRENCH, Psychoanalyt. Quart. **7**:319 (July) 1938.

Seven patients after ventriculographic examination presented peculiar and complete akinesia. Each had a tumor localized in the region of the third ventricle. After the ventriculographic procedure there were no spontaneous movements; even the eyes were not moved, and the winking reflexes were not obtainable. The patients could not eat spontaneously and were incontinent of urine and feces. Their consciousness was not disturbed. They were able to answer questions and to give information about their feelings, experiences and dreams. The cause of the akinesia seemed to be localized in the hypothalamic region. Patients with this disturbance have in common with waking persons clear consciousness and intact reality-testing ability. They have in common with sleeping persons a complete lack of initiative and will power; a passive attitude and indifference; a lack of response to stimuli from the outer world; a widthdrawal of libidinal interest from reality, and an external position of quiet, emotionless and happy rest. The bodily ego feeling is absent, and the akinetic person has no knowledge of this lack. Thus, the akinesia is to be compared with partial bodily sleep. These observations make clear the possibility of dissociating the cognitive and the volitional aspects of the ego's synthetic activity.

PEARSON, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

TRAUMATIC EPILEPSY. J. E. PATERSON, Tr. Med.-Chir. Soc. Edinburgh, 1939, p. 81; in Edinburgh M. J., July 1939.

Paterson cites an instance in which a child fell from a wall during a convulsion and later was admitted to the hospital as having traumatic epilepsy. The physician had failed to elicit the proper sequence of events. It is sometimes difficult therefore in getting a history to learn whether there has been a causal relationship between the trauma and the epileptiform manifestations. Figures show a comparatively low percentage for convulsive disturbances after concussion. The cicatricial change in the brain and meninges resulting from trauma is not the only factor in the production of such epilepsy. Something predisposes certain patients toward epilepsy, for there may be a family tendency in traumatic epilepsy almost as definite as that in idiopathic epilepsy. The author quotes Cobb, who reported a study of the incidence of epilepsy among parents, siblings and children, showing the following figures: in a control group of relatives of nonepileptic persons the incidence was 2.6 per thousand; in relatives of patients with idiopathic epilepsy there were 21 per thousand; in those of traumatic epilepsy there were 14 per thousand. There may exist in the patients in question a physiologic instability of the cerebral blood vessels, and in traumatic epilepsy a vasomotor reflex occurs which is secondary to traction by the scar tissue. Foerster, of Breslau, Germany, and Penfeld, of Montreal, Canada, have well explained the pathologic basis of epilepsy following an injury to the head. After the immediate results from the

trauma there remains slowly developing sclerosis, which ends in a fibrous scar with many blood vessels in a framework of neurologic and connective tissue. This becomes adherent to the meninges and goes deep into the brain tissue and ventricle. The ventricular wall is thereby pulled toward the surface, which must be regarded as providing noxious stimuli to convulsions. The roentgen picture helps in the diagnosis of traumatic epilepsy when focal symptoms originate in the area of the cortex underlying a lesion of bone and when there is also deformity of the ventricles. However, the diagnosis must sometimes be made on much less evidence, since a superficial scar in the cortex may cause epilepsy and give a normal encephalogram.

NEFF, Kansas City, Mo.

OCULAR DISTURBANCES IN LITTLE'S DISEASE. H. BÉGUÉ, M. BRISSOT and J. MAILLEFER, Bull. Soc. d'opht. de Paris **50**:602 (Dec.) 1938.

Reports are found in the literature of involvement of the ocular musculature in from 30 to 44 per cent of cases of Little's disease. The authors report on the examination of 27 infants. Ten had normal eyes, 5 had myopia, 7 had nystagmus, 8 had convergent strabismus and 2 had divergent strabismus. Two patients had bilateral atrophy of the optic nerve. A discoloration of the papilla was found in 22 per cent. In agreement with other reports, 37 per cent had strabismus. Fournier considered the ocular defects as stigmas of hereditary syphilis. The authors ascribe a more important role in the genesis of this syndrome to difficult labor followed by asphyxia, to tuberculosis, epilepsy, vesanic heredity by consanguinity and finally to diseases which develop during the first year of life.

A bibliography accompanies the article. L. L. MAYER. [ARCH. OPHTH.]

SYNDROME DUE TO CICATRICIAL COMPRESSION OF THE SCIATIC TRUNK; OPERATION; IMPROVEMENT. MARCULESCU and GAVRILESCU, Bull. Soc. de pédiat. de Iasi **9**:45, 1938.

The interesting feature of this case is that injections of calcium into the buttocks of a child 6 years old caused sufficient irritation and subsequent scarring to compress and interfere seriously with the function of the sciatic nerve. Fortunately the muscular atrophy and changes in sensation were properly interpreted, and after freeing of the nerve at operation recovery took place.

LESLIE, Evanston, Ill.

HEMIATROPHY OF THE FACE AND ITS TREATMENT. F. ZATLOUKAL, Časop. lék. česk. **76**:553 (May 7) 1937.

A short review of the literature is followed by a report of 5 cases. Facial hemiatrophy is characterized by atrophy of the soft parts and the splanchnocranium, involvement of half the face and facial asymmetry. Congenital and acquired types are recognized. The acquired types are divided into those due to pressure of pathologic processes in the soft parts, traumatism and surgical or general treatment; those *ex inactivitate* in cases of paresis of the facial nerve; those due to disease of the jaw bone, and those due to essential hemiatrophia facialis progressiva. The condition in the first case followed pressure due to a wide scar. In the second it was due to pressure following a lupus scar. In the third it followed scleroderma scar formation, and in the remaining 2 it was essential progressive facial atrophy. The author stresses painstaking care of the tissues to obtain the best cosmetic results. Tube grafts from the abdomen and transplants of fat, cartilage and bone were used.

STULIK, Chicago.

SPONTANEOUS SUBARACHNOID HEMORRHAGE. EUGEN LYNGAR, Nord. med. tidskr. **16**:1974 (Dec. 17) 1938.

The diagnosis of subarachnoid hemorrhage is based on the finding of blood in the spinal fluid (xanthochromia and erythrocytes). During life it is difficult

to tell the source of the bleeding. Traumatic lesions must be excluded. A sudden onset and signs of gradually increasing intracranial pressure together with signs of meningeal irritation are the most characteristic features. Fever, papilledema and retinal hemorrhage are common. The cause varies. The author reports 14 cases in 2 of which the patients were children, 9 months old and 3 years old, respectively. In both cases the cause of the disease remained unknown. Both children recovered.

WALLGREN, Göteborg, Sweden.

Psychology and Psychiatry

ELECTROENCEPHALOGRAPHIC ANALYSES OF BEHAVIOR PROBLEM CHILDREN. HERBERT H. JASPER, PHILIP SOLOMON and CHARLES BRADLEY, Am. J. Psychiat. **95**:641 (Nov.) 1938.

Seventy-one children suffering from various anomalies in behavior were studied. Abnormalities in brain potentials were found in 71 per cent. The ages of these children varied from 2 to 14 years, with a mean of 11 years. There were 12 girls and 59 boys. Thirty-nine per cent of the group showed epileptiform electrical reactions. In these patients characteristic mental and emotional disturbances generally referred to as indicating epileptic personality were in evidence. In only 2 of these cases was epilepsy suspected prior to the electroencephalographic studies, and none of the patients were having convulsions at the time of the examination.

The authors conclude that, although the fundamental nature of this analysis of the brain is not as yet fully understood, the findings are important in the evaluation of prognosis and treatment.

JAHR, Omaha.

FUNCTIONAL NERVOUS IMBALANCE IN CHILDREN. H. T. NEXBIT, South. M. J **32**:754 (July) 1939.

Nexbit describes a group of children having in common evidence of faulty utilization of calcium, postural defects, increased neuromuscular irritability, functional disturbances, exhaustion, behavioristic abnormalities and a lack of ability to adjust to usual environmental circumstances.

The need of supplying calcium to these functionally handicapped children was stressed.

SCHLUTZ, Chicago.

SOME CONSIDERATIONS CONCERNING CONGENITAL NEUROPSYCHIATRIC CONDITIONS. R. S. CRISPELL, South. M. J. **32**:757 (July) 1939.

Crispell states that a consideration of congenital neuropsychiatric conditions is important because of their frequency. He distinguishes five groups of factors or influences causing these conditions, working singly or in combination: hereditary (pregerminal), germinal, intrauterine, intranatal (birth) and early postnatal.

The subject is of importance and to the fore at present because of the possibility of its being of politicoeconomic significance and application. This is true because of the present discussion as to the socialization of medicine and because of the work and agitation concerning the subject that are coming out of Germany. The subjects of heredity and genetics are related to that of constitution. Physicians stand in need of caution and of more scientific knowledge before they can successfully deal with concrete situations in which they might make applications of knowledge of these subjects.

Attention should be focused on the factors underlying the disease rather than on the disease itself. The subject of diseases due to inheritance demands a knowledge of heredity and genetics. There is no satisfactory classification of hereditary neuropsychiatric diseases, but present knowledge permits acquisition of certain helpful guiding principles. Structural changes and functional changes may be inherited. In addition, predispositions may be inherited, complicating the subject and raising the problems of polymorphism and dissimilar heredity.

At the same time, inherited predispositions are of great neuropsychiatric interest because both in theory and in practice their manifestations can be kept sometimes, if not often, latent and not manifest and by means that are at the disposal of the neuropsychiatrist. SCHLUTZ, Chicago.

JUVENILE DEMENTIA. L. BOVET, Ztschr. f. Kinderpsychiat. **5**:33 (July) 1938.

The case of a 4 year old girl with dementia is given in detail together with a discussion of the subject in general. This is an excellent article and should be read in the original. JAHR, Omaha.

FEARS OF CHILDHOOD. H. KRAMPFLITSCHEK, Ztschr. f. Kinderpsychiat. **5**:45 (July) 1938.

The psychology of the fear instinct in its various ramifications is discussed. JAHR, Omaha.

BODILY DEFECTS AND THEIR RELATION TO EMOTIONAL DEVELOPMENT. H. MENG, Ztschr. f. Kinderpsychiat. **5**:65 (Sept.) 1938.

Thirty persons with bodily handicaps were studied in detail as regards their emotional equipment. The group included children and adults whose physical defects ranged from the various congenital deformities to crippling conditions acquired in early or in late childhood, following certain diseases, such as Little's disease, poliomyelitis, severe rickets and muscular dystrophy. Meng comes to the inevitable conclusion that physical defects have a definite effect on the emotional life of the child. Such a child is susceptible to "nervousness" in all its various manifestations. This is particularly the case with those whose misfortune came on late in childhood.

Particular stress is laid on the importance of mental hygiene in the treatment and general care of these patients. Early encouragement and an effort to instil self confidence in the victim constitute one of the greatest needs. Emphasis on the subject's abilities, with a minimum of reference to the handicap, will go a long way in helping these patients toward finding a place for themselves in a competitive world. JAHR, Omaha.

AMAUROTIC HYSTERIA FOLLOWING TRAUMA TO THE SKULL. W. BARTSCHI, Ztschr. f. Kinderpsychiat. **5**:77 (Sept.) 1938.

A 12 year old boy suffered from an injury to the left temporal region of the skull, which was followed by unconsciousness for a week. There was apparently a complete recovery, and the boy was dismissed from the hospital. Three or four weeks after this dismissal there developed severe supraorbital pain on the left side, and the boy began to complain of visual disturbances. Pressure over the orbit was accompanied by severe pain, and closure of the right eye was described as producing "black" in the left one. With the exception of a minor visual defect in both eyes the results of the examination were essentially negative, as were the observations on the spinal tap and spinal fluid.

The boy was definitely unadjusted educationally and socially, though his intelligence was not particularly impaired. His amaurosis responded to social and psychotherapeutic measures. JAHR, Omaha.

IMPORTANCE OF EARLY DIAGNOSIS OF FEEBLE-MINDEDNESS. HOLGER NYGAARD, Nord. med. tidskr. **16**:1573, 1938.

Children with a mild degree of mental deficiency get along without particular difficulties except in formal education at school, whereas they soon go astray socially when they leave school and have to pull through by themselves. Feeble-minded school children should therefore be submitted to a mental examination, and their psychic condition should be properly diagnosed in order to place them in suitable positions when they leave school. In that way a social aberration might be avoided. WALLGREN, Göteborg, Sweden.

Diseases of the Genitourinary Tract

FUNCTIONAL CAPACITY OF THE UNDESCENDED TESTIS. C. E. REA, Arch. Surg. **38**:1054 (June) 1939.

A detailed study is presented of the functional capacity of the undescended testis, with special reference to its potentialities for the production of spermatozoa. It is generally recognized that the anatomic results of surgical treatment are good, but little is reported about the function of the organ after its placement in the scrotum. Rea has shown that the undescended testis does not differ grossly or histologically from the normal up to puberty, but after this it undergoes degenerative changes. From a review of the literature it is estimated that 10 per cent of untreated human cryptorchids remain fertile. Clinically it has been proved that as high as 82 per cent of cryptorchids treated by orchiopexy have active spermatozoa in the semen. Treatment for undescended testis may be deferred until the ninth to the eleventh year. Treatment with a gonadotropic substance may be tried first, but if no results are apparent within six months orchiopexy should be performed.

Rea concludes that the undescended testis, whether untreated or treated by orchiopexy, never attains the full functional capacity of the normally descended organ as far as the production of spermatozoa is concerned. However, the value of orchiopexy in promoting the development of the undescended testis has been proved in both natural and experimentally produced cryptorchids.

KAISER, Rochester, N. Y.

THE TREATMENT OF HYPOGONADISM IN THE ADOLESCENT MALE. BRUCE WEBSTER, J. Pediat. **13**:847 (Dec.) 1938.

The use of testosterone propionate in 6 cases of adolescent hypogonadism is reported. Increased genital growth and development of the secondary sexual characteristics usually associated with normal puberty followed treatment. The optimum dose of testosterone propionate necessary to bring about or maintain puberty was difficult to determine, but 25 mg. three times a week seemed adequate. Webster has been unable to determine whether treatment with this drug must be continued for life but concludes that small maintenance doses should be given in order to maintain libido, growth of hair and the various other functions apparently dependent on a normal level of androgenic hormones in the blood.

RAUH, Cincinnati.

MANDELIC ACID THERAPY. M. F. CAMPBELL, New York State J. Med. **38**:1257 (Oct. 1) 1938.

Mandelic acid marks a notable advance in the treatment of nontuberculous bacillary urinary infections. Since acidosis develops readily in children, it is wise to start with slightly less than the average dose of mandelic acid. The urine must be carefully and periodically checked for evidence of renal irritation, but the treatment need not be stopped because of faint traces of albumin or a relatively few scattered casts. Mandelic acid is contraindicated in renal irritation and when renal function is impaired. Nausea, vomiting and diarrhea may occur.

AIKMAN, Rochester, N. Y.

PROTEIN IN THE TREATMENT OF NEPHRITIS. J. D. S. CAMERON, Edinburgh M. J. **46**:386 (June) 1939.

In this Honyman Gillespie lecture, delivered at Edinburgh, Cameron states that until quite recently the kidney had received all the attention, and the body was allowed to die around it. There is no danger from the use of protein in treatment at any time in nephritis, though the amount might be reduced at the onset of acute nephritis or in the terminal uremia of chronic nephritis. Biologically, a first class protein is needed at all stages for the nutrition of the

patient, and the supplying of this protein is more necessary than attention to the renal condition. Cameron concludes with the statement that protein starvation is more rapidly fatal than an excess of protein.

NEFF, Kansas City, Mo.

INTRAVENOUS UROGRAPHIC PROCEDURES FOR INFANTS AND CHILDREN. E. SORREL and J.-E. MARCEL, Bull. Soc. pédiat. de Paris **36**:742 (Dec.) 1938.

Films illustrating many anomalies of the urinary tract demonstrated by intravenous urographic examination of patients from 3 months to 15 years of age are reproduced, with pertinent comment. This method of investigation is recommended for all infants and children who are suspected of having urologic abnormalities.

BENJAMIN, Montreal, Canada.

CLINICAL AND ANATOMIC STUDY OF PRECOCIOUS MACROGENITALISM (PELLIZZI'S SYNDROME). JEAN LHERMITTE, Bull. Soc. pédiat. de Paris **36**:761 (Dec.) 1938.

The subject of precocious development of the genitalia and premature appearance of secondary sexual characteristics is reviewed. Autopsy observations by the authors are added to those of others to prove that this condition is not directly connected with tumors of the pineal gland or with the pituitary gland but rather results from abnormalities of the vegetative centers in the midbrain, in the region of the floor of the third ventricle

BENJAMIN, Montreal, Canada.

ENURESIS AND SPINA BIFIDA OCCULTA. J. L. DA FONSECA, Pediatria prat. **9**:333 (July-Aug.) 1938.

The literature on the relation of spina bifida occulta to enuresis is reviewed, and the author feels that in any case of persistent enuresis in a child over 7 years of age roentgen investigation should be done if the condition fails to respond to medical treatment. According to the references cited, a fairly high percentage of children in such cases show spina bifida occulta in the region of the fifth lumbar or that of the first sacral vertebra. The symptoms are presumably due to pressure of fibrous bands, and it is the division of these bands at operation which is supposed to relieve the symptoms in favorable cases. The author presents no cases of his own. He concludes his discussion with both favorable and unfavorable replies to a questionnaire which he sent out to colleagues.

DIETRICH, Beverly Hills, Calif.

RENAL SCLEROSIS IN THE CHILD. G. CAREDDU, Riv. di clin. pediat. **37**:385 (May) 1939.

An 8 year old boy had been in the hospital for two months with tetanus, followed by bronchopneumonia and empyema. Eight days after discharge he returned with fever, cough, vomiting and dyspnea. The outstanding feature was cardiac decompensation, from which he died fifty-one days later. The blood pressure had been between 70 and 130 mm. of mercury. At postmortem examination the heart was found to be as expected, but the kidneys were surprisingly large and swollen, and showed scarring from old infarcts. On histologic section they showed zones of scarring with obliteration of the glomeruli and tubules and obliterating endarteritis.

HIGGINS, Boston.

RESULTS OF AN OPERATION FOR CRYPTORCHIDISM. WESSEL and ECKHARD, Deutsche Ztschr. f. Chir. **251**:235 (Nov.) 1938.

An operation for cryptorchidism is described, together with the results in 56 cases. The elective age is 8 to 11 years in the absence of endocrine disturbances. Glandular therapy should follow operation to insure growth of the testes.

HARRIS, Durham, N. C.

LIPOID NEPHROSIS AND PNEUMOCOCCIC PERITONITIS. CARL FRIDERICHSEN, Nord. med. tidskr. **15**:704 (April 30) 1938.

The author reports a case in which voluminous edema rapidly disappeared after administration of a diet rich in vegetables, fruits and egg yolk. An accidental acute infection was followed by deterioration and development of pneumococcic (type X) peritonitis which ended fatally. Of 140 cases of nephrosis collected from current medical periodicals, death occurred in 52.

WALLGREN, Göteborg, Sweden.

Diseases of the Ductless Glands; Endocrinology

CLINICAL EXPERIENCE WITH GLOBIN INSULIN. L. BAUMAN, Proc. Soc. Exper. Biol. & Med. **40**:170 (Feb.) 1939.

The clinical trial of globin insulin (Reiner, L.; Searle, D. S., and Lang, E. H.: *Proc. Soc. Exper. Biol. & Med.* **40**:171, 1939) was made on 25 patients with diabetes of various degrees of intensity. In practically every case a single dose of globin insulin would regulate moderately severe and mild diabetes. Fair regulation was possible in several whose condition was uncontrollable with protamine insulin. The single dose was 145 units. When hypoglycemic reactions occurred, they occurred late in the afternoon, the material having been given thirty to forty-five minutes before breakfast. Cutaneous reactions were never encountered.

HANSEN, Minneapolis.

INSULIN PREPARATIONS WITH PROLONGED ACTIVITY: I. GLOBIN INSULIN. L. REINER, D. S. SEARLE and E. H. LANG, Proc. Soc. Exper. Biol. & Med. **40**:171 (Feb.) 1939.

Insulin mixed with globin produced prolonged hypoglycemia in dogs, human beings and rabbits. When zinc was added, the hypoglycemia was twice as long as that observed with standard insulin containing the same amount of zinc. In rabbits hypoglycemia following globin insulin was most intense in a few hours after injection and gradually disappeared but was not as prolonged as that produced by protamine zinc insulin.

HANSEN, Minneapolis.

THE JUVENILE FORM OF THE ADRENO-GENITAL SYNDROME. J. S. RICHARDSON and W. R. S. DOLL, Brit. M. J. **1**:501 (March 11) 1939.

The rarity of the adrenogenital syndrome in children before the age of puberty is stressed. A typical case is reported. The points of special interest, briefly discussed, are the early onset of recognizable signs, the correlation of a strongly positive ponceau-fuchsin staining reaction with an increased excretion of urinary androgens, and a postoperative increase in the excretion of urinary androgens.

ROYSTER, University, Va.

TETANY IN A SUCKLING. C. FRIDERICHSEN, Lancet **1**:85 (Jan. 14) 1939.

A case of tetany in a 5 month old infant is reported in which it was definitely demonstrated that the hypocalcemia was due to overproduction of parathyroid hormone in the mother.

For the infant the value for serum calcium was 6.7 mg. and that for blood phosphatase 0.12 mg. per hundred cubic centimeters. (The value for blood phosphorus was not reported.) For the mother the value for serum calcium was 16.4 mg., that for blood phosphorus 2.5 mg. and that for blood phosphatase 0.9 mg. per hundred cubic centimeters.

Roentgen examination of the mother's skeleton revealed evidence of osteitis fibrosa, and an adenoma of the parathyroid was removed at operation.

The infant did not show signs of tetany while fed exclusively on the mother's milk. This can be explained by the fact that the phosphorus in the mother's blood compensated for the lack of calcium.

Roentgen examination of the infant's carpus and ulnar epiphysis showed that the development of the osseous nuclei corresponded to that of a 17 month old child.

LANGMANN, New York.

SOME ENDOCRINE DISORDERS OF CHILDHOOD. R. W. B. ELLIS, Practitioner **142**: 463 (April) 1939.

One the basis of the history and physical examination, obesity can usefully be classified as follows, although clearly the distinctions are by no means rigid:

1. Primarily exogenous. In this type, excessive food intake and lack of exercise are the outstanding factors. The patients respond particularly well to limitation of the diet and increased activity.

2. Primarily endogenous. In this type a "personal factor" is suggested by, for instance, the family history, onset at puberty or a normal caloric intake. 3. Due to gross endocrine dysfunction. It cannot be emphasized too strongly that this type is by far the least common. Four subtypes may be recognized: (*a*) hypothyroidism, (*b*) hypopituitarism (Fröhlich's syndrome), (*c*) pituitary basophilism (Cushing's syndrome) and (*d*) hyperadrenalism.

Infantilism may be defined as a uniform delay in growth and development; the affected subjects have not only the height and weight but the relative proportions proper to an earlier age period.

In exact contrast to infantilism, precocious sexual and physical development is occasionally seen in young boys, giving rise to the syndrome of macrogenitosomia, the so-called "infant Hercules."

GELSTON, San Francisco.

MACROGENITALISM. M. LESNÉ, Bull. Soc. pédiat. de Paris **37**:21 (Jan.) 1939.

A boy who was first noted to have hypertrophied genitalia and general somatic overdevelopment at 1 year of age was operated on when 28 months old. A benign tumor the size of a large pea, situated between the right internal carotid artery and the stalk of the pituitary gland, was excised. At 7½ years he still showed gigantism and enlarged genitals and was mentally retarded but had apparently acquired a taste for music.

BENJAMIN, Montreal, Canada.

PARATHYROID TUMORS AND OSTEITIS FIBROSA CYSTICA. M. MEISEL, Frankfurt. Ztschr. f. Path. **51**:104, 1938.

Meisel illustrates the modern point of view regarding the relation between tumor of the parathyroids and generalized osteitis fibrosa cystica by presenting 3 cases. Most writers recognize changes in the parathyroids as the cause of von Recklinghausen's disease of the bones, while others point out that this disease is caused by a pluriglandular disorder. The author believes that, despite the close interaction between all endocrine glands, the existence of a single endocrine dysfunction is not precluded. According to many opinions, changes in the parathyroids are a significant feature of von Recklinghausen's disease of the bones, and by these the latter is distinguished from other diseases of bone. Many investigators tried to produce von Recklinghausen's disease experimentally by injecting parathyroid extract or by creating hyperacidity of the blood, but they obtained only changes somewhat resembling von Recklinghausen's disease, never the true disease. The cause of von Recklinghausen's disease is apparently not a change in metabolism alone but the presence of associated parathyroid tumor. In the author's first case the blastoma was a lymphangiectatic chief cell adenoma, in the second case a papillary chief cell adenoma and in the third case a mixed adenoma. In all 3 cases only a single tumor of one parathyroid was present.

OTTO SAPHIR. [ARCH. PATH.]

EFFECT OF PINEAL FUNCTION ON FERTILITY AND ON THE FETUS. T. MESAKI, Jap. J. Obst. & Gynec. **20**:11 (Jan.) 1939.

Injection of pineal extract into immature rabbits caused decrease in growth. When the animals later became pregnant, gestation was prolonged, the body weight of the fetuses was increased and the weight of the fetal testicles and ovaries was decreased.

When the pineal gland was extirpated, opposite results were obtained. Increase in body weight was rapid; pregnancy was shortened; the size of the fetuses was increased, and the weight of the fetal testicles and ovaries was increased.

ADAIR and POTTER, Chicago.

Diseases of the Muscles, Bones, Joints and Lymph Glands

EARLY DIAGNOSIS OF CONGENITAL DISLOCATION OF THE HIP. H. A. T. FAIRBANK, Brit. M. J. **1**:607 (March 25) 1939.

The diagnosis of congenital dislocation of the hip can be made before walking is begun. Unfortunately the condition is rarely recognized until about the eighteenth month, at which time the surgeon sees it. The longer the delay in diagnosis the less apt the child is to have a perfect cure. If it is recognized before the twelfth month, operative intervention is rarely necessary. Simple abduction for several months will effect a cure in 90 per cent of the cases. After the twelfth month forcible abduction is necessary, and in the end results are far from good. Mothers not infrequently notice one of the cardinal signs—asymmetry—and more frequently the mother takes the child to the orthopedist than to another physician. Asymmetry and obliteration of the gluteal fold on one side and shortening of the leg are the outstanding cardinal signs. The author cites a number of other diagnostic theories, but the whole article would have to be read for this to be appreciated. The differential diagnosis is described, and in the end a plea is made for early diagnosis and prompt treatment.

ROYSTER, University, Va.

A CASE OF MALIGNANT GRANULOMA ASSOCIATED WITH MILIARY TUBERCULOSIS. R. PACHIOLI, Riv. di clin. pediat. **37**:398 (May) 1939.

A boy of 7 years had what was interpreted as typical malignant granuloma (Hodgkin's disease). During the course of this there occurred fatal disseminated miliary tuberculosis, accelerated by the existing primary disease. The occurrence of both the giant cells of tuberculosis (Langhans) and the giant cells of granuloma (Reed-Sternberg cells) afforded opportunity for histologic comparison.

HIGGINS, Boston.

TREATMENT AND PROGNOSIS OF ACUTE HEMATOGENOUS OSTEOMYELITIS. J. J. NIERSTRASZ, Nederl. tijdschr. v. geneesk. **83**:2212 (May 13) 1939.

During the last ten years 143 patients with acute hematogenous osteomyelitis have been treated in the Groningen Surgical Hospital, with a mortality of 17.4 per cent. The advantages of conservative treatment in the acute stage are brought forward. By both statistical and clinical evidence and by theoretic considerations incision of the subperiosteal abscess is shown to be the best way of treatment, superior to trepanation of the bone marrow with trephine or chisel. A few factors decisive for the prognosis are discussed. For babies and young children the prognosis is decidedly less favorable than for patients at puberty.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Eye

THE SIGNIFICANCE OF ERRORS OF REFRACTION IN CHRONIC BLEPHARITIS OF CHILDREN. E. J. SOMERSET, Brit. J. Ophth. **23**:205 (March) 1939.

The purpose of this paper is to inquire into the significance of refractive errors as an etiologic factor in chronic blepharitis or blepharoconjunctivitis. All the children forming the basis of this study were referred from hospitals and clinics in London and elsewhere after they had undergone treatment generally for a long period. They were patients who had not responded to treatment in the outpatient department. In many instances correct glasses had been prescribed at the hospital or clinic without materially affecting the course of the disease. An analysis of the findings on refraction, with atropine cycloplegia, of the eyes of 300 children between the ages of 2 and 13 years, follows: There is no significant difference in the spherical refractive error in children suffering from blepharitis in comparison with the normal child. The incidence of astigmatism is similar in children with blepharitis and normal children. Children with uniocular ametropia do not show blepharitis more frequently in the eyes with ametropia. Causes other than errors of refraction must be sought for in cases of blepharitis in children.

W. ZENTMAYER. [ARCH. OPHTH.]

A FAMILY WITH COLOR BLINDNESS. A. M. VIANNA, Ann. d'ocul. **175**:901 (Dec.) 1938.

As it is not common to encounter a family in which in successive generations there are persons with color blindness, an appreciable number of them being females, it seemed of interest to report the genealogy of the Morgado family of Portugal. It was found that consanguinity played an important role.

The history is given, with charts, without which the article does not lend itself to abstracting.

S. H. MCKEE. [ARCH. OPHTH.]

GANGLIONEUROSCHWANNOSPONGIOBLASTOMA OF THE ORBITAL CAVITY. J. MONTPELLIER, P. TOULANT and J. FOISSINI, Ann. d'ocul. **176**:18 (Jan.) 1939.

This article is of interest as it concerns a malignant tumor of the orbital nerve, the occurrence of which is extremely rare, and also because two biopsies done at an interval of eight months showed two different types of neoplasm.

The report concerns a young Arab of 8 years who was seen in June 1937 for exophthalmos of the left eye, which had been progressing for two months without any functional trouble. The movements of the eye were entirely preserved, the pupillary reflexes were normal, vision was equal to that of the other eye, and the fundus was normal. No tumor could be found on palpating the orbit, nor could any enlarged glands be found. General examination gave negative results. An exploratory examination of the orbit disclosed a solid tumor adherent to the upper side of the orbit. This was removed in two parts, and for a month the patient received roentgen therapy.

He was seen again in February 1938, as the exophthalmos had increased with extreme ocular pain. Owing to the rapidity with which the exophthalmos was increasing, exenteration of the orbit was done with considerable difficulty on March 3. Roentgen treatment was again continued. Up to the time of the report the patient had remained in good health.

A detailed description of the two biopsy specimens is given. The first specimen obtained showed a tumor corresponding in structure to a malignant ganglioneuroma, while the second showed the picture of gliosarcoma. Considerable discussion of this finding follows with a bibliography.

S. H. MCKEE. [ARCH. OPHTH.]

THE BEST AGE FOR OPERATION FOR STRABISMUS. E. DUHAMEL, Bull. Soc. d'opht. de Paris **50**:352 (June) 1938.

Contradictory answers to the question of the preferred age for the operative correction of strabismus have been given by various oculists. Some of them believe that correction is easier to perform on the infant; others believe that binocular single vision is thus favored.

Asmus, Duane and Rönne recommend operation as soon as strabismus is apparent. Jaensch does not hesitate to operate on infants 1 year of age. Priestly Smith operates on children 2 years of age. Dimmer and Elschnig operate when the child is between 4 and 6 years of age. Trousseau waits until the child is between 7 and 12 years of age, while Onfray prefers the age of 10. De Lapersonne considers between 10 and 11 to be the most opportune time, and Heimann is partial to 5 years. Barck waits until the age of 12. Wendell Reeber prefers the fourteenth year. Schweiger and Czermak operate between the fourteenth and sixteenth years.

It would seem that operation for squint is done for two reasons. It is done for a purely cosmetic reason, and the vision of the amblyopic eye does not increase; it is also done on the assumption that binocular single vision may be secured. From an exhaustive study of the question, Duhamel recommends that if a purely cosmetic effect is to be the purpose of operation it is best to defer it until after puberty. For obtaining functional binocularity, he thinks that the sooner operation is accomplished the better.

A bibliography accompanies the article.

L. L. MAYER. [ARCH. OPHTH.]

DIKTYOMA OF THE CILIARY BODY. P. SATANOWSKY and E. CRAMER, Arch. de oftal. de Buenos Aires **13**:523 (Oct.) 1938.

The authors refer to the rare reports of diktyoma in the literature. The tumor occurs mostly in persons between the ages of 1 and 8 years and has its origin from the nonpigmented layer of epithelium of the ciliary body, which proliferates outward in chains of longitudinal cells that roll up on themselves and form cavities. It differs from glioma in that it does not invade the differentiated retina, expands outward and does not produce metastases. Histologic examination of an enucleated buphthalmic eye with ciliary staphylomas from a girl 6 years of age is reported.

C. E. FINLAY. [ARCH. OPHTH.]

FAMILIAL OCCURRENCE OF CONGENITAL MICROPHTHALMOS. F. K. LEYDHECKER, Arch. f. Ophth. **139**:790 (Dec.) 1938.

The pedigree of a German family is reported in which congenital microphthalmos occurred in 8 persons belonging to 5 consecutive generations. In those of the affected persons who reached the age of 40 a noninflammatory form of glaucoma developed which did not respond to treatment. The pedigree shows that the inheritance of congenital microphthalmos follows the dominant mode.

P. C. KRONFELD. [ARCH. OPHTH.]

KERATOPLASTY ATTEMPTED ON A BABY WHOSE CORNEAS WERE DESTROYED BY GONORRHEAL OPHTHALMIA. Z. NIŽETIĆ, Klin. Monatsbl. f. Augenh. **101**:32 (July) 1938.

In a 4 month old girl there was extensive destruction of both corneas, with perforation due to sloughing of the center, through which opening cortical substance and shreds of iris tissue protruded. The midwife had delayed rational treatment of the gonorrheal ophthalmia by omitting the use of the Credé method of treatment. Nižetić undertook keratoplasty for special reasons, but without much hope. General narcosis was induced with ethyl chloride and chloroform. After bilateral canthoplasty, sutures were placed below and above the limbus, so as to counteract any pressure on the perforated eyeballs. The remaining cornea

of each eye was removed with a hand trephine and Graefe's knife, and a layer was formed for the transplant, taken from the eyes of a premature infant delivered in a state of asphyxia. The prolapsing cortical substance and tissues of the iris were removed. Since no other possibility of fixation was offered, the lids were closed by sutures. The transplants became opaque, but the process of sloughing was stopped by this operation. Future developments will be reported later.

K. L. Stoll. [Arch. Ophth.]

Familial Ptosis and Ophthalmoplegia of the Supranuclear Type: Report of Cases. J. Scharf, Klin. Monatsbl. f. Augenh. **101**:71 (July) 1938.

Congenital ptosis with or without ophthalmoplegia has been reported by several authors, and Bielschowsky proved that paralysis of fixation as a congenital anomaly was of supranuclear origin. Scharf reports on 3 of 5 children of the same generation in a family with congenital ptosis and incomplete paralysis of fixation. Their ocular symptoms correlated completely, and the supranuclear location of the lesion was evident. The 2 sisters were 25 and 39 years of age, respectively, and the brother was 29. Bell's phenomenon was present in each of them. The sisters presented myopic astigmatism, and the brother, emmetropia. The function of the ocular muscles is described and discussed in detail in connection with the innervation, and a résumé of allied theories is given. Satisfactory results were obtained with the operation for ptosis after the method of Hess and Elschnig, as illustrated by pictures. K. L. Stoll. [Arch. Ophth.]

Strabismal and Other Ocular Diversities in Monozygotic Twins: Report of a Case. G. Jancke, Klin. Monatsbl. f. Augenh. **101**:76 (July) 1938.

The relatives of monozygotic twin girls born in November 1936 observed transient strabismus, alternating with periods of several weeks in which no strabismus was noticed. Squint was allegedly never observed in any other member of the family. The right eye of each twin was the leading eye and had normal vision, while the vision in the left eye of one twin was reduced to 5/15 and that in the left eye of the other twin was reduced to 5/7.5. After reporting his findings and citing the literature in point, Jahncke draws the following conclusions: The fundi of the twins showed concordance except for medullary fibers in one eye of one twin. The fusion was discordant during observation, with possible undulations of fusion; hereditary lability of fusion of a low degree was present. One of the twins presented an absence of binocular and stereoscopic vision. Discordance of the position of the eyes was manifested, as one twin was spontaneously able to overcome convergent strabismus, whereas the other showed continued divergence. Amblyopia of a minor degree did not cause permanent strabismus in one twin in the presence of normal fusion. Jancke thinks that strabismus may alternate between convergence and divergence in the same person.

K. L. Stoll. [Arch. Ophth.]

Congenital Symmetric Anomalies of the Eyes. A. Fazakas, Klin. Monatsbl. f. Augenh. **101**:257 (Aug.) 1938.

Fazakas describes in detail a number of congenital anomalies of the lacrimal apparatus. For correct function of the lacrimal apparatus it is paramount that the tear points should be at the most elevated location of the surroundings, namely, at the apex of a triangle formed by the line of the meibomian glands and the upper margin of a fold adjoining the caruncle. Interferences are found in the location of the tear points and canaliculi. The latter may be unusually long, or the lower canaliculus may be bifurcated. Hypertrophy of the frontal process of the maxillary bone produced dislocation of the fossa of the lacrimal sac in some cases. Lateral displacement of the orbits was another cause of lacrimal dysfunction. These and other anomalies are discussed. K. L. Stoll [Arch. Ophth.]

Skin Diseases; Allergy

LOSS OF SUBCUTANEOUS FAT OF THE LOWER EXTREMITIES (LIPODYSTROPHY). J. A. BIGLER, J. A. M. A. **112**:627 (Feb. 18) 1939.

Lipodystrophy involving the lower extremities is reported in a girl 12 years old. The localized loss of fat was definitely limited to the portion of the legs below the middle third of the thighs. HEERSMA, Kalamazoo, Mich.

CHARACTER OF PHOSPHOLIPID (ACETONE INSOLUBLE) FATTY ACIDS OF SERUM IN INFANTILE ECZEMA. A. E. HANSEN, Proc. Soc. Exper. Biol. & Med. **41**:205 (May) 1939.

The serum lipids of 7 infants with severe generalized eczema were determined by a microgravimetric method. The phospholipid (acetone-insoluble) fatty acids were found to be more unsaturated and to have higher average molecular weights than the total fatty acids. When these findings were compared with corresponding data obtained on 14 healthy infants, it was found that the phospholipid fatty acids comprised 26 per cent of the total fats in the eczematous infants and 31 per cent in the normal ones. The average molecular weights of the phospholipid fatty acids in these groups were the same and were definitely higher than those of the total fatty acids. The average iodine number of the phospholipid fatty acids was but 92.3 for the infants with eczema, whereas for the normal infants it was 112.8. Thus the degree of unsaturation of the fatty acids in each instance was higher than that of the total fatty acids. These data confirm a previous finding of the author that the iodine numbers of the serum fats tend to be lower for infants with severe eczema than for control subjects of similar ages. This study shows that the fatty acids of the phospholipid fraction partake in this reduction.

HANSEN, Minneapolis.

ABNORMALITY OF THE SKIN OF THE NECK. M. GROSS, Monatschr. f. Kinderh. **78**:187 (May) 1939.

Gross reports the case of a 3 month old infant with tremendous hyperplasia of the skin of the back of the neck. The article is illustrated with photographs.

GERSTLEY, Chicago.

CONGENITAL CUTANEOUS DEFECTS CAUSED BY A FORM OF EPIDERMOLYSIS BULLOSA. J. R. PRAKKEN, Nederl. tijdschr. v. geneesk. **83**:2440 (May 27) 1939.

A child presented when born two blisters. These blisters developed into slowly scarring cutaneous defects. Taking into consideration several other observations as found in the literature, Prakken states that this case supports the opinion that a number of congenital defects of skin may result from a form of epidermolysis bullosa congenita. How far this form is connected with the known varieties of epidermolysis bullosa hereditaria cannot yet be stated. The probability of epidermolysis congenita being in some cases the origin of congenital defects of the skin was mentioned first by Carol and Heybroek, in 1925.

VAN CREVELD, Amsterdam, Netherlands.

TREATMENT OF CUTANEOUS PRURITUS WITH INSULIN. C. G. VERVLOET, Nederl. tijdschr. v. geneesk. **83**:2728 (June 10) 1939.

Insulin has been shown to exert a great therapeutic influence in several forms of cutaneous pruritus. This probably depends on correction of the intracellular metabolism in the liver and in the kidneys. This medication is recommended for different types of itching of the skin. VAN CREVELD, Amsterdam, Netherlands.

HYDROPS IN A BABY. J. K. HUYSINGA, Maandschr. v. kindergeneesk. **8**:313 (May) 1939.

A premature infant when 4 months old showed extensive edema and a bad general condition. The edema was caused by a great decrease in the protein content of the serum. The urine was normal, and as no symptoms of cardiac insufficiency were present, nephrosis or congenital heart disease could be excluded, and this was confirmed at autopsy, five weeks later. Huysinga discusses whether this decrease in the protein content of the serum should be ascribed to prolonged malnutrition or to a primary defect of the liver which rendered the synthesis of protein impossible.

VAN CREVELD, Amsterdam, Netherlands.

Miscellaneous

HOMOLOGOUS POPLITEAL CYSTS OCCURRING IN IDENTICAL TWINS. P. D. ALLEN and P. MANJOA, New York State J. Med. **38**:1287 (Oct. 1) 1938.

These cysts occurred in twins 9 years of age. In each case a lump had first been noticed in back of the left knee just prior to admission. The only symptom was a slight pain. The location was identical in the two children. An older brother had had a similar cyst removed from his left leg three months previously. In both cases a cyst with a thick fibrous capsule was found overlying the median head of the gastrocnemius muscle. Such a cyst finds its origin in the gastrocnemius bursa and the first one to be described was that reported by Baker in 1877.

AIKMAN, Rochester, N. Y.

SULFANILAMIDE THERAPY (RESULTS AT THE INFANTS' AND THE CHILDREN'S HOSPITALS (BOSTON). B. W. CAREY JR., New York State J. Med. **38**:1531 (Dec. 15) 1938.

This article presents results of sulfanilamide therapy in 56 patients. These included 32 patients with beta hemolytic streptococcus infections, 4 with gonococcic vulvovaginitis, 6 with meningococcic meningitis and 1 with Proteus vulgaris meningitis. There were also 13 with infections of the urinary tract. Good results were obtained in 49. No alarming reactions occurred.

AIKMAN, Rochester, N. Y.

INFLUENCE OF INGESTION OF RAW AND DESICCATED PANCREAS UPON BLOOD LIPIDS DURING INFECTION. A. V. STOESSER, Proc. Soc. Exper. Biol. & Med. **40**:202 (Feb.) 1939.

In the child the plasma lipids during illness undergo changes similar to those which have been observed in the plasma lipids of depancreatized dogs maintained with insulin. When the dogs after pancreatectomy are fed raw pancreas in all diets, there occurs a rise instead of a fall in the plasma lipids. Twelve children ranging in age from 6 to 15 who harbored infections with relatively long febrile periods and for whom subnormal lipid values had been demonstrated were fed raw and desiccated beef pancreas. The plasma lipids were determined by Bloor's methods. This treatment had some influence on the lipid levels during the rather long periods of infection. The cholesterol esters rose rapidly from low to normal levels before the end of the febrile period. The free cholesterol remained practically at the same level in every case during the entire period of observation. The phospholipids made a fine recovery, which was maintained in the face of continuing infection. This is most significant, since phospholipids tend to remain at low levels well into the period of convalescence. The response of the total fatty acids, however, was not uniform.

HANSEN, Minneapolis.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

GERARD N. KROST, M.D., *President*

GEORGE F. MUNNS, M.D., *Secretary*

Regular Meeting, Dec. 19, 1939

Roentgen Study of Osseous Development in the Newborn, with Special Reference to Congenital Syphilis. DR. PHILIP L. ARIES.

Most of the viable infants born to mothers with active or latent syphilis have no symptoms or abnormal physical findings during the first weeks of life. The prognosis for life offered for the small number presenting abnormalities of a syphilitic character at birth is poor. Over half the infants born to syphilitic mothers escape infection. It is, however, a complicated diagnostic problem to recognize which infants harbor the infection, in order to institute specific therapy before lesions become manifest. The Wassermann test in the early months of life is not a reliable guide in recognizing actual infection in the infant. A positive reaction to the test in a healthy infant may only reveal immune bodies transmitted from the infected mother. After 2 months of age the test is more diagnostic of disease in the infant.

Roentgen examination of the skeletal structures of infected stillborn and viable newborn infants may reveal changes which are pathognomonic of congenital syphilis. The characteristic lesion is a widened band of increased density at the epiphysial margin, approximated by a submetaphysial zone of rarefaction of enough depth in the longitudinal axis to differentiate it from narrow lines of absorption seen in the normal bone or in other nonsyphilitic states.

The roentgenograms of the long bones of 85 normal newborn infants were examined. Fourteen per cent showed an increased density at the metaphysial margin and a line of rarefaction proximally. Each of these zones varied from 0.1 to 0.4 mm. in depth. Thirty per cent of the newborn infants of 162 mothers who received adequate antepartum antisyphilitic therapy had such a metaphysial density, 0.1 to 0.3 mm. wide, and a band of rarefaction proximally, 0.1 to 0.6 mm. wide. When the mothers had had inadequate antepartum treatment, 17 per cent of 69 babies had such shadows at the ends of the bones. Twenty-six mothers had had no antepartum treatment. The bones of the infants of 39 per cent of them revealed an increased metaphysial density, 0.1 to 0.3 mm. wide, plus an absorption band, 0.1 to 2.0 mm. wide. Absorption bands 1.0 mm. wide or over are pathognomonic of syphilitic osteochondritis.

A periosteal elevation was noted on one or more of the long bones in 16 infants, 2 to 3 months of age, who presented no other manifestations of syphilis. On follow-up examination, 15 of these babies revealed no syphilitic stigmas. One had a positive Wassermann reaction at the age of 2 months.

Lines or zones of increased density varying in width from 0.3 to 7.0 mm. and similar zones of rarefaction in the metaphysis are not due to syphilis in most instances. The cause of these variations in calcification in the metaphysis is believed to be explicable on a nutritional basis, with alterations in the rate of osseous growth.

DISCUSSION

DR. ARTHUR H. PARMELEE: Dr. Aries has followed up the work Dr. Halpern and I did some years ago. It is difficult to make a diagnosis of congenital syphilis in the newborn as one sees it today. It is quite a different disease from what it was thirty or forty years ago, because today most mothers have had some treatment. Consequently, one infrequently finds infants born of syphilitic mothers who show positive clinical signs of syphilis. These babies look like other normal babies. The usual routine Wassermann reaction is not reliable. However, some refinements are being made in the serologic tests. For example, quantitative tests are valuable in many instances in which a single ordinary serologic examination has been negative. Then too, quantitative tests are of value in ruling out the pseudoreactions which occur in some of these infants. About 25 or 30 per cent of infants born of syphilitic mothers escape syphilis whether the mother is treated or not. This is dependent on the activity of the disease in the mother during pregnancy. There is a fairly large percentage of mothers with syphilis in whom the disease is so attenuated that at no time during pregnancy is there a sufficient involvement of the placenta to cause infection of the fetus. When one is unable to make a diagnosis clinically or when serologic tests are unreliable, roentgen examination may be of help, I have found; but having struggled with roentgen diagnosis for a long time and having discovered many of its pitfalls, I am inclined at present not to recommend it for general use as an infallible diagnostic aid. A full-fledged osteochondritis should be easily recognized, but one has to acquire quite a little proficiency from experience before one can learn to interpret the minimal findings, and these are the ones that cause trouble in diagnosis. Certainly other things besides syphilis will produce widened epiphysial lines. Therefore, a definite diagnosis cannot be based entirely on an increased zone of cartilage calcification. Widened epiphysial lines are found with particular frequency in premature infants that do not have syphilis. However, I believe that if one is familiar with the phenomena of normal growth of bone, learns to interpret roentgenograms and understands syphilis, one can get a great deal of information about the newborn from roentgenograms of the long bones. Osteochondritis heals spontaneously in the majority of cases. Roentgen changes in the bones tend to disappear after the fourth or fifth month. The clinical symptoms, if present, also tend to disappear. This means that the diagnosis of congenital syphilis becomes increasingly difficult after the fourth or fifth month. It has been noticed that practically none of Dr. Aries' pictures showed periostitis. This is a later development and does not occur in the newborn period without osteochondritis, although it is occasionally associated with it. Periostitis shows in the roentgenogram after about four to six weeks, as a rule, when the hypertrophic periosteal tissue has become calcified.

DR. NOEL G. SHAW: I should like to emphasize what Dr. Parmelee said about the difficulty of making a diagnosis of congenital syphilis in a case which is not clearcut. It is known that certain of these children are infected to a varying degree. Some of them with milder infections, especially if the mother has had a few antisyphilitic treatments during pregnancy, may remain free of clinical symptoms for an indefinite period. Some of them may show signs of syphilis or have a positive Wassermann reaction or positive roentgen ray findings in the first few months or years, while others may show signs late in childhood or even in adult life. When the syphilitic mother has had no treatment during pregnancy and still no evidence of syphilis can be found when her child is first examined, at some age up to 12 years, it is true that the child may seem to be self cured or to have escaped infection. However, if this child shows unmistakable signs of congenital syphilis, such as interstitial keratitis, at the age of 12 to 15 or even later, then he had congenital syphilis all the time, even though the results of all earlier examinations may have been negative. This is a point which is rarely emphasized, and I believe one should be cautious about assuring parents after one examination of a child that he has not been infected by the mother, especially if her syphilis was active and she had less than thorough treatment the last half of pregnancy.

In the Central Free Dispensary of Chicago, where I have followed these children the past ten years, the so-called nonsyphilitic child of a syphilitic mother returns for a physical, roentgen and blood examination every three months until he is 18 months old and then every six months indefinitely for a physical examination and Wassermann test. Few of these children ever have positive Wassermann reactions, but they all should be watched.

All the help possible, including roentgen examination, is needed in making a diagnosis of congenital syphilis. However, Caffey (*Am. J. Roentgenol.* **42**:637 [Nov.] 1939) shows roentgenograms from children he believes nonsyphilitic which duplicate all the syphilitic osseous changes shown by Dr. Aries, with the exception of the saw-toothed epiphysitis and the destructive lesions in the distal ends of the diaphyses. So it remains to be seen if the osseous changes that have been associated with congenital syphilis are pathognomonic or simply evidence of marked disturbance of normal growth of bone which may occur in other diseases also.

DR. HENRY G. PONCHER: I should like to say a word about the metaphysial areas of rarefaction that Dr. Aries showed in his nonsyphilitic babies. This finding correlates with the presence of a neonatal line of hypoplasia in the enamel and dentin which appears at the time of birth and marks the transition from intrauterine to extrauterine life. Undoubtedly, the process of birth and the immediate neonatal period are accompanied by a mild metabolic disturbance which is permanently recorded in the enamel and dentin and can be seen in ground sections, while in the long bones it is transient and is only occasionally shown by the roentgen rays. In view of these facts one must be cautious, as Dr. Aries has stressed, about attributing specific diagnostic value to metaphysial rarefaction alone in the long bones of the newborn.

DR. I. M. LEVIN: The essayist is to be complimented for this careful evaluation of the roentgen findings in the bones of the newborn. I have had the privilege of treating many patients with congenital syphilis transferred from Dr. Aries' service. I can corroborate his opinion that infants showing cutaneous or osseous manifestations of syphilis within a week after birth almost invariably die. Of 67 patients with congenital syphilis treated in the children's venereal disease service of the Cook County Hospital in recent years, 22 had syphilitic findings at birth and all died except 1, who at 3 months is doing well after a stormy course.

For eighteen months I have been searching for the presence of bismuth lines in the long bones of patients with congenital syphilis who had received four weekly intramuscular injections of bismuth subsalicylate within a month, following a previous nine weeks' course of acetarsone by mouth. The roentgen studies before and after the administration of bismuth fail to reveal any suggestive lines.

The statement that a positive Wassermann reaction in the infant may be a carry-over from the mother in from 20 to 25 per cent of cases I believe to be fallacious. In my experience only about 5 per cent of infants with positive serologic reactions after birth turn out to be without syphilitic infection later. Quantitative serologic studies with decreasing titers are suggestive of lack of infection.

There is a phase in the diagnosis of congenital syphilis which is well known but not sufficiently employed—dark field examination. It has been possible to demonstrate the spirochete in nasal, cutaneous, oral and perianal lesions in a surprisingly high percentage of instances.

Syphilis is a decidedly protean disease. One often hears the statement that women with long-standing syphilis, after repeated pregnancies, may bear healthy children. At present I have a striking exception to this statement. An Italian woman gave birth to her fourteenth child, who manifested marked cutaneous, osseous and visceral syphilis. She had never had an abortion or stillbirth. Two of the 14 children died of causes not related to syphilis. The serum of the mother and of 12 children gave a 4 plus reaction, the father's alone giving a negative reaction. Careful clinical examination of 9 members of the family failed to reveal the slightest evidence of past or present syphilis.

This experience should teach one to be exceedingly cautious in making the diagnosis of syphilis.

DR. A. S. TRAISMAN: I wonder if Dr. Aries has found any infants who had no roentgen findings at birth but in whom changes in the bones developed later in life. Dr. Levin mentioned that babies who show such changes at birth die early. In the series of patients my associates and I have observed at Northwestern University, I have encountered 17 infants under 1 year of age who had roentgen findings characteristic of syphilis, which cleared up after one course of treatment with acetarsone and bismuth. Certainly, some of them must have had these changes at birth. As Dr. Parmelee has stated, many of the osseous lesions in infants disappear even without treatment.

DR. R. W. SPAETH: I conclude from the discussion of Dr. Shaw that it is hazardous to adopt a child on the basis of the results of the various serologic tests. A 3 year old boy born of a mother with a markedly positive Wassermann reaction is at present free from all signs of syphilis. He has had three negative Wassermann tests. An attorney and his wife have requested my opinion concerning the advisability of adopting this child into their own family. In view of the possibility of the appearance of syphilitic manifestations during later childhood or adolescence, despite the negative findings at present, I feel inclined to disapprove the adoption. I should like to hear the opinion of Dr. Shaw in this matter.

DR. PHILIP L. ARIES: I appreciate this interesting discussion, which brought out many things omitted or hurried over in my talk. One group of babies observed were delivered of mothers who had a 4 plus Wassermann reaction and had had no antepartum treatment and of whom many were young women with recently acquired syphilis. There were 26 such children in this series. Seven of the infants were of special interest because of the follow-up data. One baby had cutaneous lesions at birth and roentgen evidence of a markedly syphilitic osteochondritis. The baby died soon after birth. The second infant had indefinite roentgen findings at birth. When he was 4 months old, some rarefaction was noted in the metaphysial zones and the baby had a positive reaction to a Kahn test. The third child was normal on physical examination at birth. The roentgenogram of the long bones showed a zone of decreased density 8 mm. wide immediately proximal to the metaphysial margin. When he was 7 weeks old, a pseudoparalysis with a marked osteochondritis was found. The child died of syphilis at the age of 9 weeks, while receiving antisyphilitic therapy.

Three babies were normal at birth and remained so during the follow-up periods, of two months, fourteen months and three years. One infant who had questionable roentgen changes in the bones at birth was not brought in for a later examination.

The obstetricians felt better when the conclusion was reached that narrow lines of submetaphysial rarefaction could not be interpreted as being due to syphilis, because they were concerned about the efficiency of the antepartum antisyphilitic therapy administered to the mothers. The presence of such lines in the roentgenograms of the long bones of normal newborn infants settled this matter.

In answer to Dr. Traisman's question, the osseous pathologic changes which are manifest at the second month of life and later are usually not demonstrable in the newborn period. My observation, corroborated by Dr. Levin, is that the prognosis for life is poor when there is clinical or roentgen evidence of congenital syphilis during the first week of life.

Clinical Implications of Recent Studies on Anoxia and Asphyxia. DR. ERNST GELLHORN.

The studies were carried out on narcotized dogs, which inhaled from Douglas bags gases containing various oxygen-nitrogen mixtures in order to allow a quantitative study of various degrees of anoxia. Moderate degrees of anoxia elicit an increase in respiration only, without affecting the blood pressure. With decreasing oxygen concentration, the respiratory response is increased and the blood pressure rises in proportion.

The significance of the respiratory response to anoxia is evident from the fact that when the respiratory response is poor the rise in blood pressure is marked but that no alteration in blood pressure may occur when an adequate increase in respiration is observed. This rise of blood pressure is due to stimulation of the chemoreceptors of the carotid sinus and the arch of the aorta, since after their removal the blood pressure falls in anoxia, even when artificial respiration is used.

When anoxia continues for a sufficient length of time or is severe enough to prevent adequate adjustment by increased respiration, cardiac output and blood pressure, a gradual failure of circulation sets in. This prevents the removal of carbon dioxide from the tissues. Thus a condition of asphyxia, characterized by anoxia plus retention of carbon dioxide, results. Asphyxia is considered a final attempt of the organism to adjust itself to the condition of anoxia, since it results in further increase in blood pressure and respiration and more effective liberation of epinephrine than is observed in either anoxia or hypercapnia.

DISCUSSION

DR. ARTHUR H. PARMELEE: This question of anoxia and asphyxia is of great interest to those who are dealing with the problems of the newborn. There is considerable confusion in regard to the relative merits of oxygen alone or oxygen and carbon dioxide in the treatment of newborn infants with asphyxia neonatorum, and I believe I express the opinion of the majority of pediatricians when I say that my impression is that one gets as good or better results with oxygen alone. The basis of my opinion is largely the work of Schmidt. He showed that respiratory stimulants fail to work normally in the presence of oxygen want and that a stimulant that ordinarily produces stimulation of the mechanism will in the presence of oxygen want cause a reversal. If because of oxygen want the center of the medulla is not normally responsive to carbon dioxide, then the first requisite is oxygen. Another point occurs to me: I doubt if many physiologists have studied the physiology of the fetus or of the newborn infant as compared with that of the adult. The prematurely born child, for example, shows many of the characteristics of a desympathectomized animal. His vasomotor apparatus is immature. Can one expect, then, that the adjustments that Dr. Gellhorn speaks of are being made in the same degree in the premature animal or in the newborn animal, whose sympathetic system is still immature?

DR. LEON ARIES: Is the p_H of the tissues greater in the young animal or child than in the adult? Does it become more acid as the animal becomes older?

DR. I. M. LEVIN: I should like to ask if there has been any experimental work done with reference to the dilution factor of helium in oxygen. When one has a condition of anoxia due to oxygen lack, what would be the response to administration of adequate amounts of helium?

DR. ERNST GELLHORN: In reply to the first question I can say that physiologists have studied the embryo extensively. There have been publications by Snyder and Rosenfeld from Johns Hopkins University and by Barcroft in England. I think the fetus and the newborn infant in many respects act differently from the adult. I believe the carotid sinus reflexes are weaker.

So far as treatment of the newborn baby is concerned, I do not know anything about it. I just present my estimation of these conditions, which I think point to alteration in respiration as the primary defense in anoxia. Whether or not in conditions of severe and prolonged anoxia stimulation of respiration would be entirely adequate, I do not know. My experiments involve only acute anoxia of relatively short duration in narcotized animals. There are great differences between the conditions present in asphyxia of the newborn and those studied in my investigations.

GERARD N. KROST, M.D., *President*

GEORGE F. MUNNS, M.D., *Secretary*

Regular Meeting, Jan. 16, 1940

Prothrombin in the Blood of Newly Born Mature and Immature Infants as Determined by the Microprothrombin Method. DR. KATSÚJI KATO.

The hypothesis that the underlying cause of hemorrhagic diathesis in the newborn is a lack of vitamin K, which influences the level of blood prothrombin, has been advanced simultaneously by Waddell and associates (1939), Owen and associates (1939), Quick and Grossman (1939) and Nygaard (1939). Dam and Schonheyder's (1934) discovery of an antihemorrhagic factor responsible for the onset of bleeding in chicks fed on a fat-free diet suggested this theory. Additional investigations are necessary in order to substantiate this far reaching assumption.

As a preliminary step in the study of the nature of hemorrhagic disease of the newborn, it is needful first to define the limits of normal variations in blood prothrombin during the neonatal period. For the investigation of this problem a method had to be found applicable to small infants, for measuring the quantitative value either of the plasma prothrombin itself or of its convertibility in the blood-coagulating system.

The methods available for the measurement of prothrombin were: (1) Howell's prothrombin method, (2) the plasma prothrombin method of Quick, Stanley-Brown and Bancroft, (3) the whole blood method of Quick, Stanley-Brown and Bancroft, (4) the two stage titration procedure of Warner, Brinkhous and Smith and (5) the curative blood-clotting method of Dam and Glavind. But all these methods, with the exception of the third, require the use of plasma prepared from relatively large amounts of venous or arterial blood, a procedure which is inconvenient and inadvisable to use with small infants, particularly when the determinations are to be made at frequent intervals. Accordingly, a new microprothrombin test, using whole capillary blood, has been devised, following the general principles involved in Quick's plasma method. The prothrombin clotting time of normal adult whole blood as determined by this micromethod is twenty seconds, with deviations of plus or minus two seconds.

By this method the prothrombin clotting time of the blood was measured in 173 newly born infants; an aggregate of 1,595 tests was performed in duplicate. Of the total number, 100 were normal full term babies and 73 were premature infants, the birth weight of 2,500 Gm. being used as the dividing line.

The average prothrombin clotting time of mature infants was found to be forty-three and two-tenths seconds on the day of birth and to shorten gradually as the infants grew older, until by the ninth or tenth day of postnatal life the average time was in the neighborhood of twenty-five seconds. In the premature group, however, the average initial prothrombin clotting time was forty-six and five-tenths seconds; a much longer period was required than with the mature infants to stabilize the values for the prothrombin clotting time at a lower level, and they showed a much greater degree of fluctuation.

DISCUSSION

DR. HENRY G. PONCHER: Dr. Kato's microadaptation of Quick's test is a distinct advantage in dealing with infants. The range between normal variations and pathologic values is sufficiently clearcut so that there is little difficulty in interpreting values. The test can be readily carried out at the bedside or in a physician's office. The values for the newborn infant during the first four or five days of life can be stabilized at lower levels by administering vitamin K to the mother, as many workers have discovered. It has been found that this may be

accomplished by a single dose of crystalline vitamin K given orally as late as twenty-four hours before delivery or parenterally as late as eight hours before delivery. The practical value of such a procedure remains a problem for future study. The demonstration of the effectiveness of vitamin K therapy in hemorrhagic disease of the newborn, however, has been striking, for in every instance the results were clearcut and dramatic. The hypoprothrombinemia found prior to treatment was always promptly corrected. While the doses of vitamin K used will undoubtedly be revised with further experience, crystalline vitamin K has been found effective orally and parenterally. Only the patients with internal and external hemorrhage were selected for treatment. Those with milder disturbances, with only slight hypoprothrombinemia and minimal bleeding externally, were not treated and recovered spontaneously. A number of facts have emerged from this study: first, that the values for prothrombin clotting time are highest during the first four days of life; second, that they can be stabilized at lower levels by antepartum vitamin K therapy; third, that hemorrhagic disease of the newborn can be promptly and effectively treated with vitamin K.

DR. ARMAND QUICK, Milwaukee: Of particular interest to me were the favorable results obtained by giving vitamin K to the mother. It has been my finding that normally the infant is born with no store of prothrombin or of vitamin K.

My method for determining prothrombin and Dr. Kato's modification are both based on the principle that the clotting time of blood or plasma is a quantitative measure of the prothrombin, provided an excess of thromboplastin and a fixed amount of calcium are added. It is to be expected that both tests should yield the same results. It must be remembered, however, that the other commonly used method for the measurement of prothrombin, namely, Smith's test, gives results quite different from those of Dr. Kato's test and mine. Time does not permit the discussion of the reasons for the difference between these two tests. It will be arbitrarily assumed that Dr. Kato's and my results present a correct picture of the concentration of prothrombin.

If an infant is studied carefully, one finds that at birth the concentration of prothrombin is nearly normal. Then often a sudden drop occurs. Nygaard found that this decrease takes place after the tenth hour. Apparently, prothrombin is consumed in forming a clot in the umbilical stump and perhaps for other purposes. The prothrombin lost is not replaced, because the infant lacks vitamin K. The subsequent sudden spontaneous rise in prothrombin is due to the entrance of bacteria into the intestinal tract, for it is well known that bacteria synthesize vitamin K. Apparently, the more aseptically a baby is handled, the greater is the incidence of prothrombinopenia. Thus, Javert found that bleeding of the newborn occurred twice as frequently in the ultramodern New York Hospital as in the Berwind Maternity Clinic. The prothrombin deficiency of the newborn baby is, I am sure, entirely comparable to the hemorrhagic disease of the chick deprived of vitamin K. In twenty-four hours the level of prothrombin can be restored to normal, for both baby and chick respond with remarkable promptness to oral administration of vitamin K. I have found that in chicks a transfusion is far less effective, and I am sure the same is true in the case of giving blood to the baby.

There are, I think, three indications for administering vitamin K, unless one is going to give it routinely to mothers and babies: 1. The start of any bleeding in the baby. Any loss of blood brings about further loss of prothrombin, and any loss of prothrombin means more bleeding; thus a typical vicious circle is established. 2. Any emergency operation on a baby under 10 days old. The Jews placed circumcision at the eighth day, and this command is repeated again and again in the Old Testament. The question arises: Did the Jewish people learn that if they circumcised before the eighth day they ran into difficulties? 3. Difficulty in delivery with danger of intracranial hemorrhage.

There is another question that comes up. In the adult patient, the concentration of prothrombin goes down in jaundice. In a baby jaundice does not seem

to bring about a prothrombin deficiency. I have seen several babies with atresia of the common duct who yet had perfectly normal concentration of prothrombin. So far, as a source of thromboplastin the rabbit's brain apparently has no equal. The human brain also contains a fairly large concentration but is not recommended as a source. Why does the body have such a good supply of prothrombin in the lung and in the brain? Apparently it is as a protection against hemorrhage.

DR. HEYWORTH N. SANFORD: I think that Dr. Kato should be congratulated on this work in studying the coagulating elements of the blood in the newborn, but there are a few questions that I should like to ask about the conclusions that have been drawn.

First with regard to the method: This test was made by adding an excess of thromboplastin and calcium to whole blood. Therefore, this actually is not a test for prothrombin but is a measure of the conversion time of all the blood-coagulating elements plus an excess of thromboplastin and calcium. As this is not a true test for prothrombin, why go to all this trouble to show that the blood of the newborn has a slower coagulation time in the first few days of life, when the simple coagulation test of Rodda shows exactly the same thing? In fact, all that has been done by adding thromboplastin and calcium is to speed up the coagulation time of the test sample so that the results are read in seconds instead of in minutes as in the Rodda method, which increases the margin of error.

Second, I should like to ask why, if a prothrombin deficiency is the cause of hemorrhagic disease of the newborn, the lowest prothrombin levels are found at birth and in the first day of life, when hemorrhagic disease of the newborn is never observed clinically before the second or third day of life. According to the figures given, the prothrombin level is actually rising at this time.

Third, I am unable to correlate the frequency with which hemorrhagic disease of the newborn is seen as stated tonight with other observations. Ethel Dunham in a survey of the frequency of hemorrhagic disease of the newborn found its incidence to be 1 in 1,500 newborn infants. I believe that Dr. Kato stated that he found it twice in 173 infants. This makes an incidence of 1 in 85. The incidence in my own experience has been only 3 times in 10,000 newborn infants. Dr. Quick said that newborn infants that are unsterile will obtain more vitamin K and have more prothrombin than others. Perhaps this is the explanation for my babies.

Last, I should like to ask if any of these newborn infants with hemorrhagic disease or hemorrhage were untreated with vitamin K as a control. Recently I had a newborn child that began to ooze from the navel and vomited blood on the third day of life. The coagulation time (Rodda) was twenty minutes, and the prothrombin clotting time (Quick) was sixty seconds. On the following day without treatment of any kind the bleeding had stopped; the coagulation time was seven minutes, and the prothrombin clotting time was eighteen seconds.

DR. ARMAND QUICK: The superiority of the prothrombin determination over the clotting time of blood as a means of detecting danger of hemorrhage is best demonstrated by the prothrombin curve. It will be seen that the clotting time is little changed until the prothrombin has dropped below 20 per cent. Any method for determining the clotting time, such as the test employed by Rodda, will show delayed clotting when the prothrombin is below 20 per cent but will not detect a decrease of prothrombin before this level is reached. This is of particular importance in regard to the patient with jaundice. The clotting time preoperatively may be normal but the prothrombin far below normal. After operation, a further small drop of prothrombin often is sufficient to produce a hemorrhagic condition.

DR. HEYWORTH N. SANFORD: I am not criticizing your method as such. I have found it to be an excellent means of showing a prothrombin deficiency in the adult with bile obstruction, when the older methods of coagulation time will show no such change. That is a different story. What I do say is that it seems to me rather laborious to advocate doing this test on all newborn infants when the simpler coagulation time tests will give the same results.

DR. KATSUJI KATO: In reply to the last question, namely, the effect of blood transfusion or injection on the prothrombin clotting time, I may refer again to the conclusion reached by Whipple that the injection of serum was the answer to the treatment of melena neonatorum. Unfortunately, I have no personal observation on this particular phase.

In answer to Dr. Sanford's questions I may say first that the coagulation time test was formerly used in the diagnosis of hemorrhagic disease of the newborn, but the developments in our knowledge of this disease during the past year clearly demonstrate the advisability of determining the prothrombin clotting time, because it clearly and specifically brings out the deficient component in the blood-coagulating mechanism which is responsible for this disease. In other words, the prothrombin test does not replace the coagulation test; it may be regarded merely as an additional refinement of the latter test as a diagnostic procedure. I wish Dr. Quick would elaborate further on this point.

The incidence of hemorrhagic disease of the newborn is certainly not high. Nygaard reported 66 cases of this disease occurring among 9,748 infants. Statistical data coming from various sources, however, are not absolutely accurate and not strictly comparable, since the majority of the reports were published before the true etiologic factor was discovered.

The hemorrhagic manifestations of this disease always occur coincident with the prolongation of prothrombin clotting time. The data on the prothrombin clotting time in newborn infants which I have just presented merely indicate the general trend in normal babies during the early postnatal life. In hemorrhagic disease of the newborn the bleeding occurs almost invariably when the prothrombin clotting time becomes prolonged to an extremely abnormal degree. In the instance of a baby with syphilitic hepatitis, mentioned by Dr. Poncher, the initial prothrombin clotting time was about two minutes and reached the greatly abnormal time of six minutes in the three days during which the hemorrhage persisted. If one determines the prothrombin clotting time in this disease one will find that in each instance the hemorrhagic manifestations occur at the height of the prolonged prothrombin clotting time. It must be remembered that during the first three or four days of life the babies individually show great variations from day to day and possibly from hour to hour, and this explains why this disease occurs most frequently during this period of extreme prothrombin fluctuation.

Tongue-Tie in Infants and Children. DR. E. T. MCENERY and FRANCES PERLOWSKI GAINES.

The subject is presented in two phases: first, tongue-tie in the newborn in regard to nursing; second, tongue-tie in older children in regard to difficulties of speech.

Tongue-Tie in the Newborn (Dr. McEnery).—Tongue-tie consists in the presence of a short frenum with folds of mucous membrane on each side which unite the tip of the tongue to the floor of the mouth and the posterior lingual surface of the gum. At birth the tongue is always short; so it is not always easy to determine how much the frenum interferes with its movement. In a newborn child the tip of the tongue is as yet incompletely developed, and the frenum may normally be well forward. As the infant develops, the tongue becomes longer and thinner toward the tip.

In the newborn, tongue-tie is claimed to be a factor in difficulty in nursing, either at the breast or with the bottle. With the latter procedure there should be no trouble. With the breast, especially if the nipple is short or retracted, there may be some difficulty, but this can be corrected by gentle massage of the mother's nipple. It is usually due to misunderstanding of the technic of nursing that the frenum of the tongue is cut. In some smaller maternity services this seems to be almost a routine procedure.

The dangers from cutting the frenum are as follows: There may be subsequent infection at the base of the tongue with the formation of a large ulcer

and spreading stomatitis, which makes it so difficult for the baby to take food that severe dehydration and loss in weight may occur. When this ulcer at the base of the tongue heals, it often leaves a large amount of scar tissue, which makes for marked immobilization of the tongue.

Severe hemorrhage has also been reported, and considerable thought should be given before this operation is performed, especially when it is delegated to an intern. Instances have been reported in which after cutting the tongue became too movable and the baby swallowed it, with consequent attacks of asphyxia.

In a large series of newborn babies I have not seen a tongue-tie that had to be clipped. Nursing technic does not require that the short frenum be cut, and because of the dangers associated with this so-called simple operation it should not be performed.

Tongue-Tie in Older Children (Francis Gaines).—Tongue-tie is one of the most frequently advanced explanations of the causation of defective articulation. Physiologically, it arises from a thickening of the geniohyoglossi muscles meeting in the midline of the tongue and being elevated into a distinct vertical fold, called the fraenum linguae. If this vertical fold extends too far forward toward the tip of the tongue it interferes with the upward lift of the apex. The tongue is a mobile, muscular organ capable of undergoing great changes in length and width at every contraction of its muscles, and in this very capacity for change lies its great range of adjustability and compensation.

The congenitally shortened frenum is observed most by the obstetrician and pediatrician; it is generally conceded that it interferes little, if at all, with mastication, deglutition or sucking. With growth the tongue undergoes considerable elongation. In approximately 1,000 patients with disorders of speech seen in the speech clinic of Children's Memorial Hospital, there have been only 4 patients having seriously shortened frenums.

Compensatory adjustments of the highly mobile organ result in adequate and intelligible speech. Until a definite cause and effect relationship between disorders of articulation and tongue-tie can be established, operation is usually contraindicated.

If surgical intervention is employed to give the patient a freely movable apex of the tongue to aid in the production of lingual palatal sounds, it is necessary for the surgeon to bear in mind two factors: first, the necessity of preventing adhesion following the clipping and, second, the habit formation which has been going on ever since the child began to talk. The postoperative care is the surgeon's primary problem, but it is his further duty to explain to the parents the necessity of speech reeducation.

The presence of a shortened frenum is not proof that it is the factor responsible for the deviation of speech. The articulatory aspects of normal speech are dependent on many factors, such as acuity of and discrimination in hearing, speed and specialization of muscular movements, emotional attitudes and type of speech environment, all of which must be properly differentiated before it can be said, if at all, that any one factor is the cause. The presence of distorted articulation calls for careful differential diagnosis and thorough cooperation between the speech reeducator and the physician.

Book Reviews

Epidemics in Schools and Analysis of the Data Collected During the First Five Years of a Statistical Inquiry. The School Epidemics Committee. Price, 4s. 6d. net. Pp. 289, with 43 illustrations and 170 tables. London: His Majesty's Stationery Office, 1938.

This extensive study of epidemics and sickness in the children of public boarding schools of England brings out some clear definitions of problems which must be solved in order to suggest effective ways of controlling epidemic diseases and presenting loss of school time due to absences during sickness. The authors say: "What we believe we have done is to provide a large body of coordinated information sufficient to enable anyone interested in the subject to acquire a reasonably clear view of what the position is, of what problems are of importance and how they may be tackled. . . . Information . . . which has immediate practical value to those in charge of schools, is meagre. . . . No problem can be solved before it has been accurately formulated."

The data covered twenty-one boys' schools and ten girls' schools, which contained a total of over 29,000 children. The period is divided into three terms for each of five years, and much of the data is given by weeks in each term. All illness considered caused at least one day's absence from school.

Cold and influenza, as expected, accounted for a large proportion of the time lost. Girls were absent with colds much more than boys, with an average term rate of 22.6 per cent as compared with 5.6 per cent for the boys. It appears that this sex difference is one of the problems for further investigation, because the average duration of the attacks was less for the girls, and ". . . there was evidence of an inverse relationship between the attack rate and days lost per attack in the category of nasopharyngeal infection in both sexes." It is suggested that the English girls are subjected to stricter surveillance and on that account are more likely to be kept out of school. Such a difference between the care of girls and boys, of course, may result in more prompt isolation of girls and the avoidance of some secondary infections. While the authors refrain from drawing inferences or making recommendations, the question is obvious whether prompt recognition and isolation of all nasopharyngeal infection would prove to be a beneficial precaution. They raise this question again when they find boys suffering twice as frequently as girls from otitis media, two and a half times as frequently from pneumonia and eleven times as frequently from acute rheumatism.

They mention the need for data obtained by accurate reporting of every cold, whether it causes loss of school time or not, but they gravely question whether such data can be obtained. They explain with some detail the difficulties experienced in recording accurately the various infections of the respiratory tract and give the reason for their final decision to group all cases of coughs, colds and sore throat under the term "naso-pharyngeal infection." This difficulty with diagnoses makes the analysis unconvincing when the attempt is made to determine whether a previous tendency to multiple colds has any influence on subsequent experience. An apparent periodicity of colds, shown by the weekly rate of attack throughout the five years, suggests the possibility that further light might be thrown on this important subject by more rigidly controlled observations of the children. At least it is clear that one of the problems is how to obtain more accurate distinctions, which are not influenced by the idiosyncrasy of the observer.

The evidence failed to show that an attack of influenza confers any effective immunity that lasts as long as a year, although it suggested that an attack may

confer immunity which lasts for several weeks or more. The hypothesis is proposed that those who escape the first epidemic possess more natural immunity and so are more likely to resist the second outbreak.

The authors found that "just over half the boys and rather under half the girls had had their tonsils removed," and then set out to discover whether this mass attack was justified. They studied the attack rates for numerous conditions in relation to tonsillectomy. Influenza, sore throat, colds and cough rates were compared for pupils with and without tonsils, as well as the attack rates for measles in tonsillectomized and nontonsillectomized "susceptibles." It was concluded that there is no evidence whatever that wholesale tonsillectomy results in a diminished incidence of the infection. While they found reason for believing that in properly selected cases there is benefit from operation, they say that ". . . one cannot avoid the conclusion that there is a tendency for the operation to be performed as a routine prophylactic ritual for no particular reason, and with no particular results."

It is of special interest that this report is preliminary to a continuance of the inquiry. Epidemics and the medical problems of boarding schools are matters concerning which the pediatrician wants facts. While he will find no new methods of control, he will welcome the variety of data on attack rates and the epidemiologic discussion of all the more common illnesses of the age period between 13 and 18 years. The knowledge of how sickness rates vary from term to term, from year to year and from school to school, and the information on losses in school time should be useful when special problems arise.

Das Stillproblem und Vorschläge zur Besserung der Stilltätigkeit. Supplement to Archiv für Kinderheilkunde, No. 19. By Hans Helbich, M.D. Price, 2.80 marks, paper. Pp. 41, with 5 illustrations. Stuttgart: Ferdinand Enke, 1939.

Helbich in this monograph on "The Breast Feeding Problem and Proposals for the Improvement of Breast Feeding Activities" follows the well known, didactic textbook methods. The material contained is clearly presented but contains nothing new. The only original contributions by Helbich date back to 1911-1912 and concern themselves with the physiology of the secretion of milk.

The monograph is divided into five chapters. It was surprising to read in the first chapter of the decrease in Germany at the present time both in the number of breast-fed babies and in the duration of nursing. The author ascribes this decrease to the diminished ability of women to nurse babies and lists as causes: migration from country to city, poor nutrition, working conditions of girls in which lack of recreation and too little rest play great roles, smoking of cigarets and undernutrition following war conditions. However, he made the statement that nursing could be prolonged if the desire to nurse was there and the proper technic of nursing was put into effect immediately after the birth of the child.

In the second chapter he discusses proper foods, exercises and mental hygiene for the mother. In his discussion of the nutritive requirements of the nursling, he stresses the tremendous importance of breast milk and suggests other foods, such as milks and cereals, only if the baby loses weight and inanition develops. No mention is made of the necessity of giving cod liver oil, fruit juices and other foods as a routine. Five feedings a day is given as an average, but it must be stated, to Dr. Helbich's credit, that he is not a stickler for feeding by the clock. He allows one-half hour variations if the need arrives. Vomiting is mentioned as being due to overfeeding or underfeeding; no mention is made of pyloric stenosis or other pathologic conditions as possible causes of this symptom.

In chapter 3 he stresses the importance of the emptying of the breasts by the baby, the hand or the breast pump, in order to stimulate the production of milk. He also suggests putting the baby to both breasts at each feeding. Artificial feeding is discussed in a vague manner; complementary and supplementary feed-

ings are advised without specific mention of types of foods to be used. He does specifically advise against extra foods during the first three months. He states that breast feeding for at least six months is very "advisable." There is no discussion of the relative mortality of breast-fed and bottle-fed babies, which would fit very well into this chapter as a vital reason for breast feeding.

In chapter 4 there is rather frank criticism of the technic of many of the German hospitals in regard to care of the newborn. He assigns this state of affairs as the cause of the high neonatal mortality rate and links it up particularly with the lack of technic in breast feeding. It would have been interesting at this point to read a discussion of the relative position that not breast feeding the newborn played in relation to the many well recognized causes of neonatal mortality which are not even mentioned. He does, however, imply that the high neonatal mortality can be reduced by cooperation between the obstetric and the pediatric departments in certain institutions. In this chapter he also criticizes in a rather striking manner the undermanned welfare departments in the large cities and also in the villages.

In chapter 5 he pleads for better care of the infant. He criticizes the habits of the people and the speed of life. He decries the lack of education in nursing technic and in feeding of the mothers. He criticizes the education of nurses and of hospital personnel and particularly the lack of care of the newborn. He shows that welfare organizations are not satisfactory. There are poor clinical facilities, and the quarters are overcrowded and unhygienic. There is a lack of general medical care; the nurses are overworked, and there are insufficient visits to the poor. He recommends larger personnels and better trained persons for these positions. He protests vigorously against the economic necessity of mothers having to work after leaving the hospital and recommends local nursing care in every small village instead of monthly visits by nurses from the city. In view of the present political condition in Germany, this may be considered a very frank, courageous and outstanding plea for the care of infants. This attitude on the part of Dr. Helbich should be commended in spite of certain outstanding scientific errors which he has allowed himself to fall into, such as his statements that deficient breast feeding is the cause of rickets and that such foods as fruits and vegetables are more important than cod liver oil and vitamin D preparations.

All in all, this is an interesting description of the present day German attitude toward problems in breast feeding and the care of infants under the existing political system.

Pediatric Surgery. By Edward C. Brenner, M.D., F.A.C.S. Price, $10. Pp. 243, with 293 engravings. Philadelphia: Lea & Febiger, 1938.

This is the first comprehensive American work on the subject of pediatric surgery to be published since the excellent two volume edition by Kelley. Dr. Brenner has had the assistance of several collaborators, who have written sections on anesthesia, blood transfusion, cleft lip and palate, thoracic surgery, urologic conditions and neurologic surgery. Fractures and orthopedic conditions, usually so extensively treated in works on surgical pediatrics, have been purposely omitted, both in the interest of brevity and as being adequately covered in other textbooks. The section on general conditions includes taking the history, clinical and laboratory procedures, wounds and accidents, surgical shock, water balance, preoperative and postoperative care and the surgical aspects of rickets and scurvy. Brevity and conciseness have been attained by the use of well chosen words and phrases, by reference to personal experience rather than compilation of references and by a rather trenchant, didactic style which gives important subjects in sufficient detail but does not burden the text or obstruct the search for specific informaion. The omission of discussion on controversial subjects suggests at times the somewhat dogmatic tone of the clinical amphitheater, but it serves admirably to stress important points.

The discussion of appendicitis and peritonitis is excellent and may profitably be studied by all who treat these conditions. The section on conditions of the chest is exhaustive, including much which applies primarily to adults as well as certain medical conditions the surgical aspects of which are minimal. In the section on cleft lip and palate the newer methods are well presented, and attention is directed to the defects of some of the older procedures, which are still too frequently used. The importance of cooperation with the orthodontist and with the instructor in speech is stressed. The section on urology is especially commendable. It is comprehensive, minutely detailed when necessary and easily readable. Above all, it emphasizes gentleness and attention to the psychic peculiarities of children, which are of vital importance in attaining the best results.

The greater familiarity of the author with conditions in adults and with procedures for them is suggested by the inclusion of many conditions which are of rare incidence in children and by the recommendation to use such heavy material as no. 1 chromic catgut and silkworm gut retention sutures.

In spite of Dr. Brenner's protest that the volume is not compendial, it will be found of great value for ready reference because of the fact that, except for the intentional exclusion of orthopedics, it covers with commendable detail all the commoner surgical conditions encountered in infants and children and refers briefly to the rarer ones. The text is well illustrated and indexed; the composition of the volume is excellent, and the use of frequent captions in bold face type and of numerous cross references to related chapters facilitates the search for any desired subject.

Otolaryngology in General Practice. By Lyman G. Richards, M.D. Price, $6.00. Pp. 352, with 72 illustrations. New York: The MacMillan Company, 1939.

This volume will prove of considerable value to physicians in pediatric or in general practice who wish an authoritative and not too technical statement of the best present day authority in this field. It not only will give them the benefit of recent advances but should equip them much better for examinations of and therapeutic procedures on the ear, nose and throat that may come within their own practice.

The style could be more terse, but the book is readable. Sketches and diagrams, not burdened with too much detail, are clear, graphic and numerous and make the text easily understood. Fine points of technic are well explained and illustrated in detail, so that they are easily grasped. The author apparently expects the general practitioner to be proficient in some procedures usually allocated to the otolaryngologist. This can be done, as he states, only if the physician masters the use of the head mirror and illumination so that he works with clear vision.

Considerable attention is paid to conditions of interest to the pediatrician. Especially valuable sections are those on nasal allergy, sinal disease in children and respiratory obstruction, with discussion of intubation and tracheotomy.

The approach to the subject is made by a discussion of the symptoms, but there is a brief but adequate discussion of anatomy and pathology also.

The volume is well worth reading and will serve as a useful textbook for consultation as special problems arise in the field it covers.

Raquitismo en la infancia. By Enrique Sujoy. No price given. Pp. 265, with 90 illustrations. Buenos Aires: 1936.

This is an excellent study of clinical and experimental rickets, reviewing the history, pathology, etiology, clinical symptoms and treatment of rickets. It is as thorough as any textbook that has appeared in English. The plates and photographs are well chosen, and the subject matter is up-to-date. There is a comprehensive bibliography of foreign literature.

Blood Groups and Blood Transfusion. By Alexander S. Wiener, M.D. Second edition. Price, $5. Pp., XVII, 306, with 52 illustrations and 86 tables. Springfield, Ill.: Charles C. Thomas, Publisher, 1939.

This book may be used as a laboratory manual, so precise and so thorough is the author's presentation of detail. Its outstanding characteristic, however, is the scholarly exposition of biologic observations and their application to problems in the fields of medical therapy, anthropology and medicolegal practice.

The Merck Index: An Encyclopedia for the Chemist, Pharmacist, Physician, Dentist and Veterinarian. Fifth edition. Price, $3. Pp. 1060, with no illustrations. Rahway, N. J.: Merck & Co., Inc., 1940.

The fifth edition of the Merck Index, for 1940, has just appeared. This is a peculiarly complete list of drugs used in medicine and many others, with useful information regarding the sources of these drugs and their therapeutic usage and dosage.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

American Committee:

Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
General Secretary: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Assistant Secretary-Treasurer: Dr. Charles F. McKhann, 300 Longwood Ave., Boston.

Canadian Committee:

Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston, Mass. Time: Postponed indefinitely.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria. Corso Bramante 29, Torino 120, Italy.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

British Paediatric Association

President: Prof. Charles McNeil, 44 Heriot Row, Edinburgh, Scotland.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

SOCIEDAD CUBANA DE PEDIATRÍA

President: Dr. Clemente Inclan Costa, Manrique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Jorge Muñoz Turnbull, Av. Alvaro Obregón 186, Mexico, D. F.
Secretary: Dr. Fernando López Clares, Medellín 191, Mexico, D. F.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Secretary: Dr. Hugh L. Dwyer, 315 Alameda Rd., Kansas City, Mo.
Place: New York. Time: June 10-14, 1940.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. J. B. Bilderback, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Hotel Peabody, Memphis, Tenn. Time: Nov. 18-20, 1940.
Region I. Place: Mayflower Hotel, Washington, D. C. Time: April 4-6, 1940.
Region II. Place: Richmond, Va.
Region III. Place: Hotel Muehlbach, Kansas City, Mo. Time: May 16-18, 1940.
Region IV. Place: Seattle, Wash. Time: May 30-June 1, 1940.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S HOSPITAL SECTION

Chairman: Miss Mabel Binner, Children's Memorial Hospital, Chicago.
Secretary: Winifred Culbertson, Children's Convalescent Hospital, Cincinnati.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Herbert B. Wilcox, 39 E. 75th St., New York.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Place: Skytop, Pa. Time: May 2-4, 1940.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. L. M. Lindsay, 815 Medical Arts Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

Society for Pediatric Research

President: Dr. Daniel C. Darrow, 330 Cedar St., New Haven, Conn.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.
Place: Skytop Lodge, Skytop, Pa. Time: Afternoon of May 1 and morning of May 2, 1940.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. R. Cannon Eley, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. Frederick Fischer, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. C. L. Lyons, Paulsen Medical-Dental Bldg., Spokane, Wash.

Rocky Mountain Pediatric Society

President: Dr. John Schoonover, Republic Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.
Secretary: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables, Fla.

STATE

Alabama Pediatric Society

President: Dr. Stewart H. Welch, 1117 S. 20th St., Birmingham.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.

Arkansas State Pediatric Association

Chairman: Dr. G. D. Murphy, 112 Peach St., El Dorado.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Harold K. Faber, 2341 Clay St., San Francisco.
Secretary: Dr. Hartzel H. Ray, 23–2d Ave., San Mateo.

Florida State Pediatric Society

President: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables.
Secretary: Dr. George N. Leonard, 605 Lincoln Rd., Miami Beach.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. L. H. Muse, 384 Peachtree St. N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Business Meeting. Place: Savannah. Time: April 1940.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Oliver L. Stringfield, 1416 Bedford St., Stamford.
Secretary: Dr. Joseph L. Hetzel, 103 N. Main St., Waterbury.
Time: Three meetings a year.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. H. William Elghammer, 5307 Hyde Park Blvd., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: Peoria. Time: May 22, 1940.

Indiana State Pediatric Society

President: Dr. O. N. Torian, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

Louisiana State Pediatric Society

President: Dr. Phillip C. De Verges, Audubon Bldg., New Orleans.
Secretary-Treasurer: Dr. W. C. Rivenbark, 220 Physicians and Surgeons Bldg., New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester.
Secretary: Dr. Leslie O. Ashton, 850 Park Ave., New York.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. John M. Higgins, 600 S. Wilbur Ave., Sayre.
Secretary: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Allan L. Richardson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. Ward L. Chadwick, 524 Medical Arts Bldg., Grand Rapids.

Mississippi State Pediatric Society

President: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. Herman M. Jahr, 1120 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. Elmer W. Bantin, 440 Aquila Court Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Marion Y. Keith, 369 N. Elm St., Greensboro.
Secretary: Dr. G. W. Kutscher Jr., 176 Woodfin St., Asheville.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. Ben H. Nicholson, 301 W. 12th St., Oklahoma City.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.
Secretary-Treasurer: Dr. William Weston Jr., 1428 Lady St., Columbia.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. William E. Van Order, 546 McCallie Ave., Chattanooga.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.

TEXAS PEDIATRIC SOCIETY

President: Dr. T. A. Tumbleson, 2100 North St., Beaumont.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Dallas. Time: May 15, 1940.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. W. Ambrose McGee, 616 W. Grace St., Richmond.
Secretary: Dr. John M. Bishop, Medical Arts Bldg., Roanoke.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. J. L. Blanton, 207 Fairmont Ave., Fairmont.
Secretary: Dr. Theresa O. Snaith, 450 Center Ave., Weston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. N. C. Wetzel, 2103 Adelbert Rd., Cleveland.
Secretary: Dr. Fred Rittenger, 10515 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. T. B. Verner, 170 St. George St., Toronto, Canada.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry S. Altman, 940 Grand Concourse, New York.
Secretary: Dr. David Zahn, 2474 Valentine Ave., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Benjamin Kramer, 6 Pierrepont St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank van der Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. Gerard N. Krost, 2376 E. 71st St., Chicago.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. Edgar Loomis, 351 W. Jefferson Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. William O'Donnell, 1553 Woodward Ave., Detroit.
Secretary: Dr. Robert Mason, 5140–2d Blvd., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Stephen C. Redd, 157 Forrest Ave. N. E., Atlanta.
Secretary: Dr. C. Dixon Fowler, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Thomas J. Donovan, 3820 Fannin St., Houston, Texas.
Secretary: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. John Aull, 1103 Grand Ave., Kansas City.
Secretary: Dr. George Herrman, 1107 Bryant Bldg., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. H. R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Paul M. Hamilton, 248 E. Main St., Alhambra, Calif.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Benjamin Stoloff, 1149 Eastern Parkway, Brooklyn.
Secretary: Dr. Harry Apfel, 988 Park Pl., Brooklyn, N. Y.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., second Monday of each month, October to March, inclusive.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. James Dobbins, 42-04 Ditmars Blvd., Long Island City, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. Harry H. Donnally, 1612 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Harry A. Spigel, 2647 Connecticut Ave. N. W. Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of October, January, February, March and April.

Memphis Pediatric Society

President: Dr. Barton Etter, 376 S. Bellevue St., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. S. F. Morgan, 5630 N. Lake Dr., Milwaukee.
Secretary-Treasurer: Dr. F. R. Janney, 1411 Wauwatosa Ave., Wauwatosa, Wis.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Rustin McIntosh, Babies Hospital, New York.
Secretary: Dr. Leslie O. Ashton, 850 Park Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Roland E. Nutting, 205 W. 2d St., Duluth, Minn.
Secretary-Treasurer: Dr. John M. Adams, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Every month, except June, July and August.

Philadelphia Pediatric Society

President: Dr. Pascal F. Lucchesi, 4000 N. Front St., Philadelphia.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. E. R. McClusky, 3200–5th Ave., Pittsburgh.
Secretary-Treasurer: Dr. Carl Ruder, 646 Washington Rd., Mount Lebanon, Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

Richmond Pediatric Society

President: Dr. Charles L. Outland, 312 N. 9th St., Richmond, Va.
Secretary-Treasurer: Dr. T. Stanley Meade, 913 Floyd Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Secretary: Dr. W. L.. Bradford, 16 N. Goodman St., Rochester, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee. Time: Second Friday of each month.

St. Louis Pediatric Society

President: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Secretary-Treasurer: Dr. Peter G. Danis, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society Bldg. Time: Third Friday of ech month from September to June.

Seattle Pediatric Society

President: Dr. Jay I. Durand, 1305–4th Ave., Seattle.
Secretary: Dr. Frederick B. Joy, 1215–4th Ave., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. E. Earl Moody, 829 S. Alvarado Ave., Los Angeles.
Secretary: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Yark Osterlin, Central Michigan Children's Clinic, Traverse City, Mich.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Time: Nov. 15-16, 1940.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. M. Bernard Brahdy, 531 E. Lincoln Ave., Mount Vernon.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Ave., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October December, February and April.